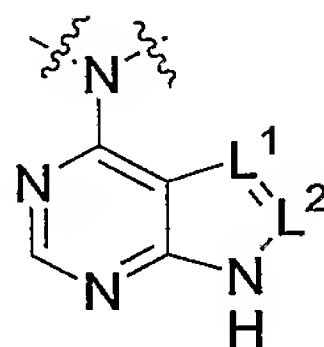


Claims

We claim:

- 5 1. A compound comprising one or more phosphonates and a substructure of formula I:



I

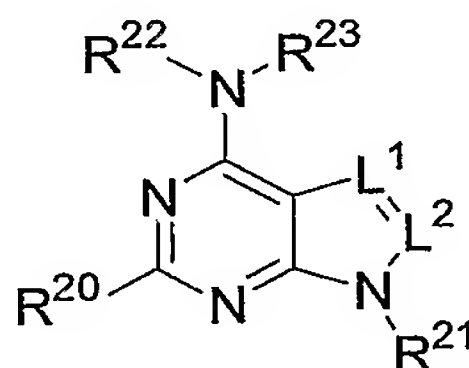
wherein  $L^1$  and  $L^2$  are -N- or -CR<sup>a</sup>-; and

R<sup>a</sup> is hydrogen, alkyl, substituted alkyl, aryl or substituted aryl;

10

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 that comprises a substructure of the formula:



15 wherein:

$L^1$  and  $L^2$  are independently -N-, or -CR<sup>a</sup>-, provided that only one of  $L^1$  or  $L^2$  is a nitrogen atom;

R<sup>a</sup> is hydrogen, alkyl, aryl or substituted aryl;

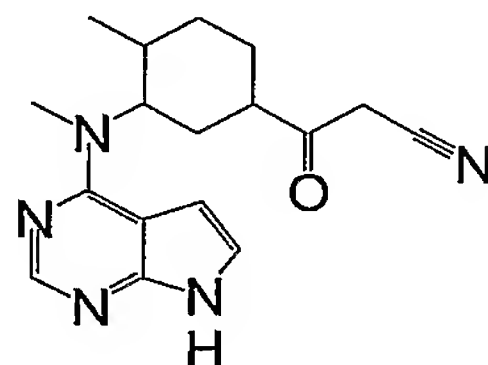
20 R<sup>20</sup> is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl aryl, cycloalkyl, substituted aryl, or -NR<sup>b</sup>R<sup>c</sup>;

R<sup>b</sup> and R<sup>c</sup> are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or aralkyl;

R<sup>21</sup> is hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, substituted alkyl, aryl, substituted aryl, aralkyl, or substituted aralkyl; and

$R^{22}$  and  $R^{23}$  are independently hydrogen, alkyl, substituted aryl, or aralkyl.

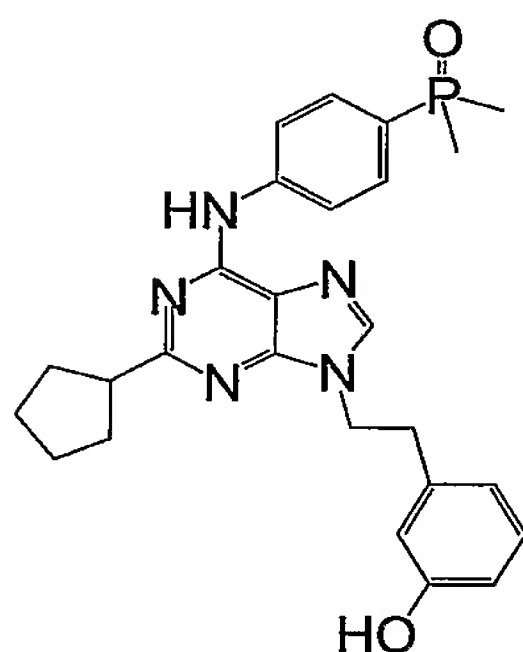
3. The compound of claim 1 that comprises a substructure of formula II:



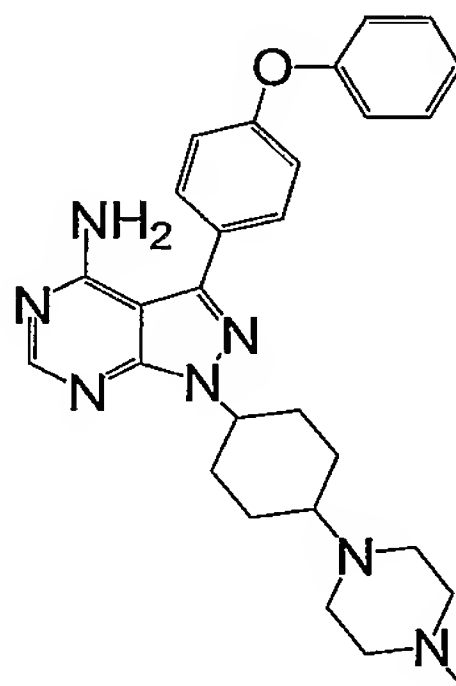
5

II

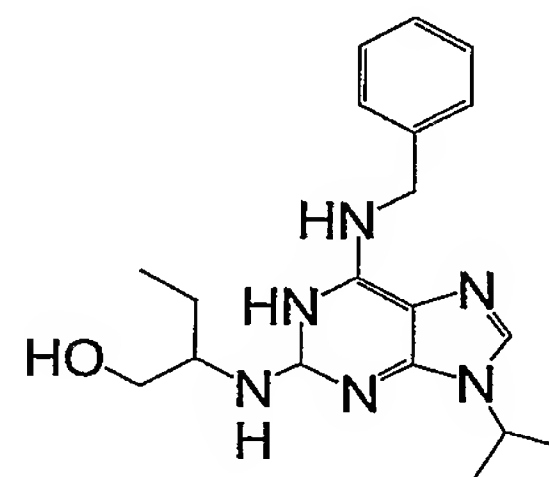
4. The compound of claim 1 that comprises a substructure of formula IIIa, IVa or Va:



IIIa

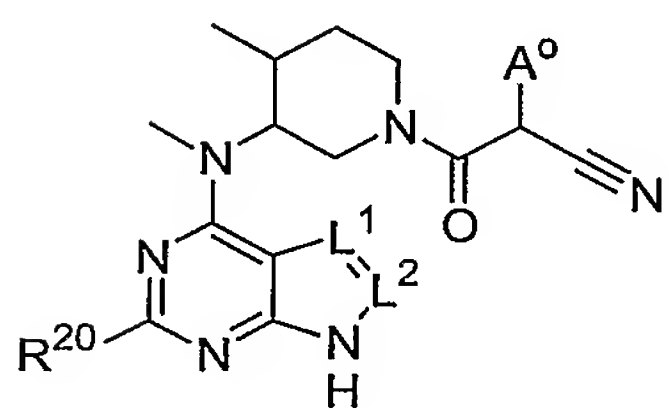


IVa

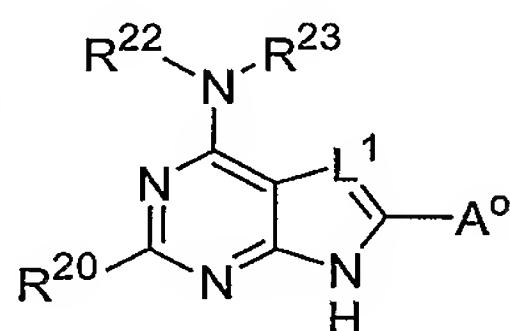


Va

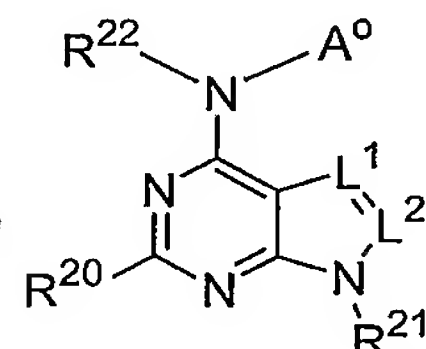
- 10 5. The compound of claim 1 having formula 1, 2, 3, or 4:



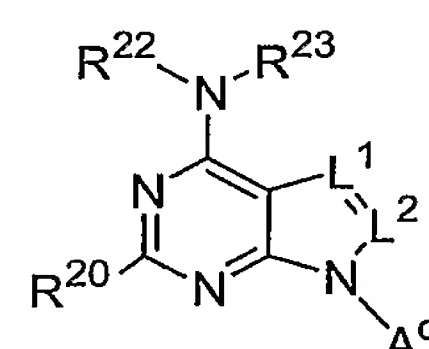
1



2



3

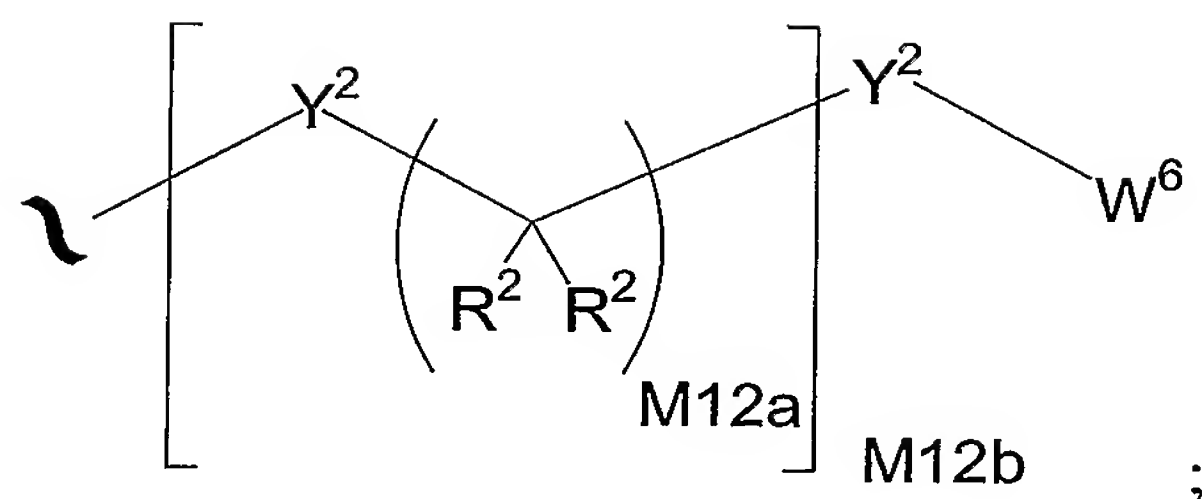


4

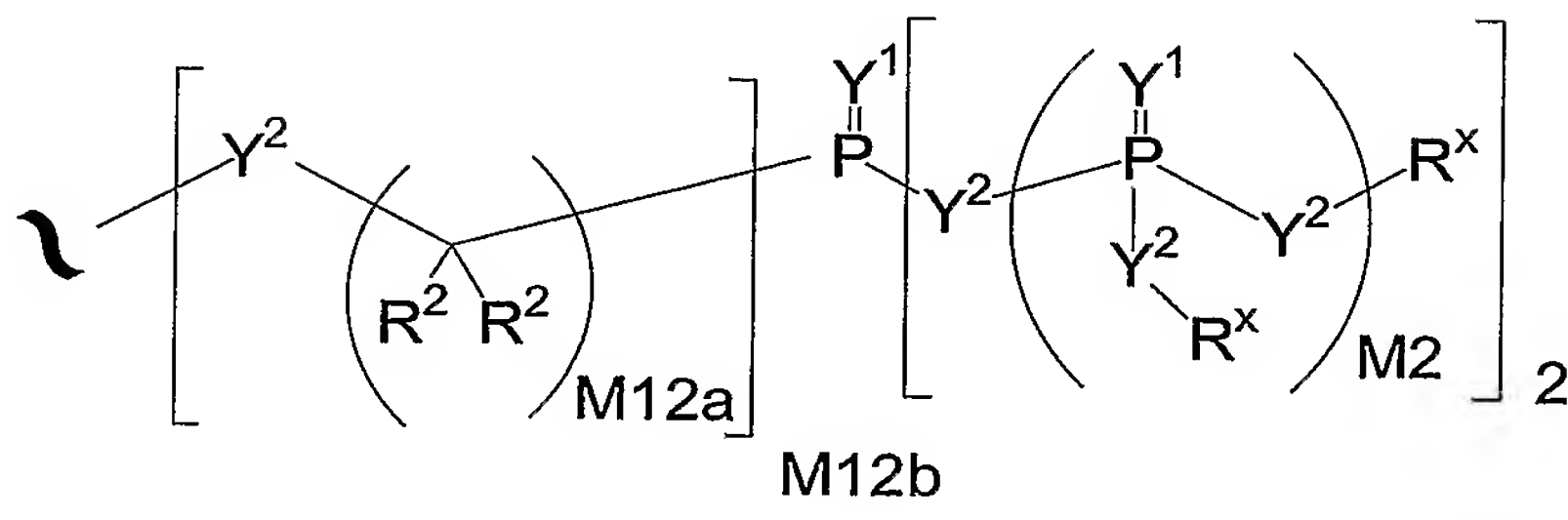
wherein:

$A^0$  is  $A^1$ ;

15  $A^1$  is:



$A^3$  is:

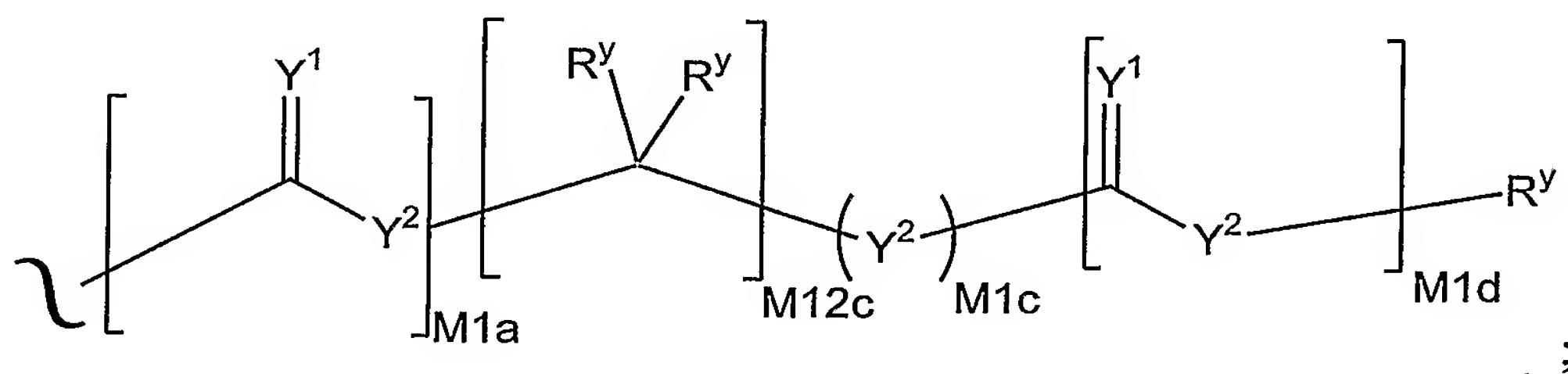


$Y^1$  is independently O, S,  $N(R^x)$ ,  $N(OR^x)$ , or  $N(N(R^x)(R^x))$ ;

Y<sup>2</sup> is independently a bond, O, N(R<sup>x</sup>), N(OR<sup>x</sup>), N(N(R<sup>x</sup>)(R<sup>x</sup>)), or -

S(O)<sub>M2</sub>-; and when Y<sup>2</sup> joins two phosphorous atoms Y<sup>2</sup> can also be C(R<sup>2</sup>)(R<sup>2</sup>);

R<sup>x</sup> is independently H, R<sup>2</sup>, W<sup>3</sup>, a protecting group, or the formula:



$R^y$  is independently H,  $W^3$ ,  $R^2$  or a protecting group;

R<sup>2</sup> is independently H, R<sup>3</sup> or R<sup>4</sup> wherein each R<sup>4</sup> is independently

15 substituted with 0 to 3 R<sup>3</sup> groups;

$R^3$  is  $R^{3a}$ ,  $R^{3b}$ ,  $R^{3c}$  or  $R^{3d}$ , provided that when  $R^3$  is bound to a heteroatom, then  $R^3$  is  $R^{3c}$  or  $R^{3d}$ ;

R<sup>3a</sup> is F, Cl, Br, I, -CN, N<sub>3</sub> or -NO<sub>2</sub>;

$$R^{3b} \text{ is } Y^1;$$

$R^{3c}$  is  $-R^x$ ,  $-N(R^x)(R^x)$ ,  $-SR^x$ ,  $-S(O)R^x$ ,  $-S(O)_2R^x$ ,  $-S(O)(OR^x)$ ,  $-S(O)_2(OR^x)$ ,  $-OC(Y^1)R^x$ ,  $-OC(Y^1)OR^x$ ,  $-OC(Y^1)(N(R^x)(R^x))$ ,  $-SC(Y^1)R^x$ ,  $-SC(Y^1)OR^x$ ,  $-SC(Y^1)(N(R^x)(R^x))$ ,  $-N(R^x)C(Y^1)R^x$ ,  $-N(R^x)C(Y^1)OR^x$ , or  $-N(R^x)C(Y^1)(N(R^x)(R^x))$ ;

5  $R^{3d}$  is  $-C(Y^1)R^x$ ,  $-C(Y^1)OR^x$  or  $-C(Y^1)(N(R^x)(R^x))$ ;

$R^4$  is an alkyl of 1 to 18 carbon atoms, alkenyl of 2 to 18 carbon atoms, or alkynyl of 2 to 18 carbon atoms;

$R^5$  is  $R^4$  wherein each  $R^4$  is substituted with 0 to 3  $R^3$  groups;

$W^3$  is  $W^4$  or  $W^5$ ;

10  $W^4$  is  $R^5$ ,  $-C(Y^1)R^5$ ,  $-C(Y^1)W^5$ ,  $-SO_2R^5$ , or  $-SO_2W^5$ ;

$W^5$  is carbocycle or heterocycle wherein  $W^5$  is independently substituted with 0 to 3  $R^2$  groups;

$W^6$  is  $W^3$  independently substituted with 1, 2, or 3  $A^3$  groups;

$M2$  is 0, 1 or 2;

15  $M12a$  is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

$M12b$  is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

$M1a$ ,  $M1c$ , and  $M1d$  are independently 0 or 1;

$M12c$  is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

20  $L^1$  and  $L^2$  are independently  $-N-$ , or  $-CR^a-$ , provided that only one of  $L^1$  or  $L^2$  is a nitrogen atom;

$R^a$  is hydrogen, alkyl, aryl or substituted aryl;

$R^{20}$  is hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl aryl, cycloalkyl, substituted aryl, or  $-NR^bR^c$ ;

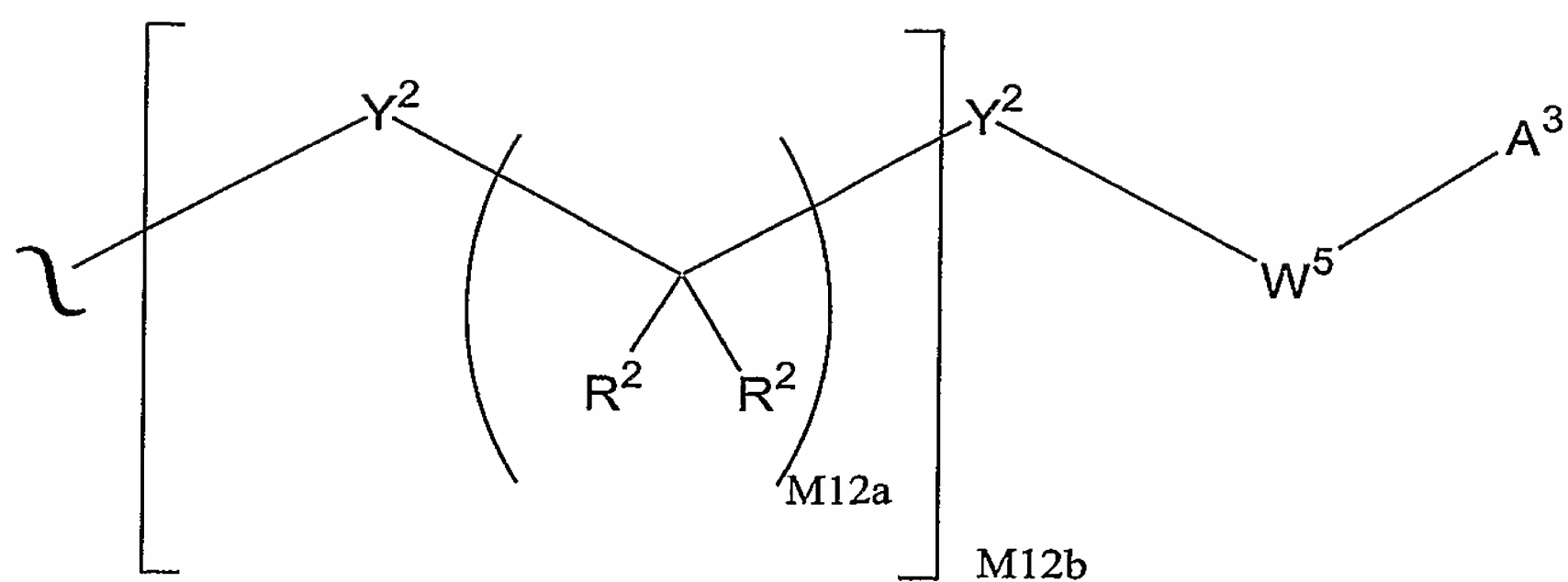
25  $R^b$  and  $R^c$  are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or aralkyl;

$R^{21}$  is hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, substituted alkyl, aryl, substituted aryl, aralkyl, or substituted aralkyl; and

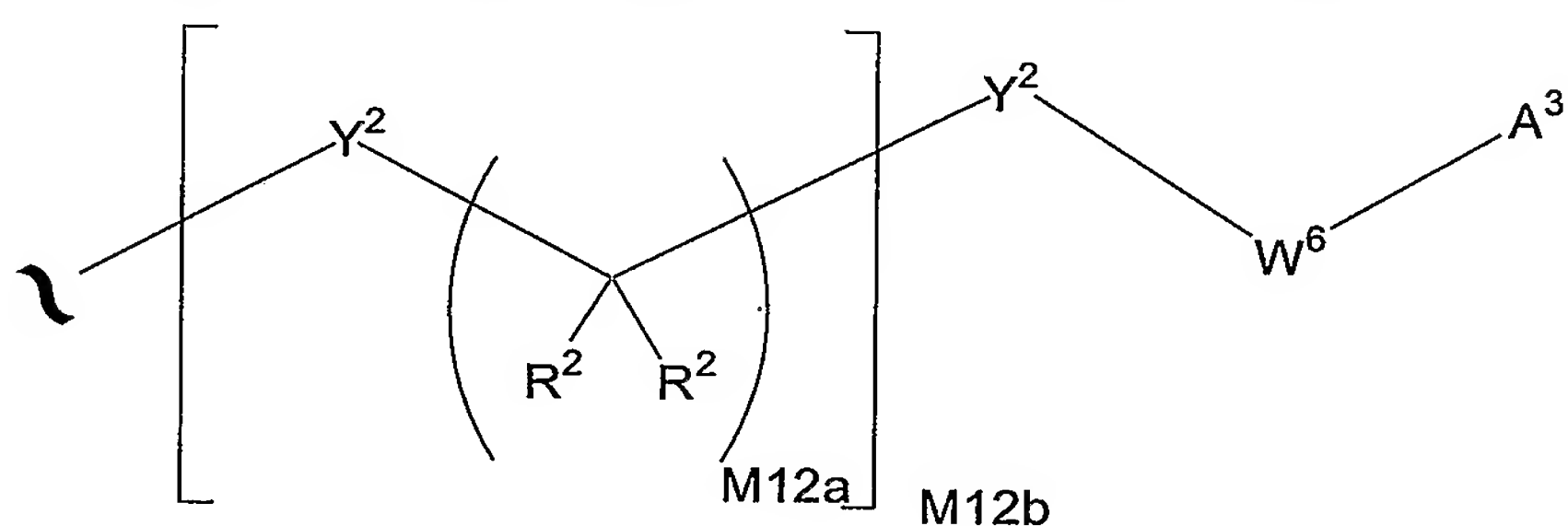
$R^{22}$  and  $R^{23}$  are independently hydrogen, alkyl, substituted aryl, or aralkyl.

30

6. The compound of claim 5 wherein  $A^1$  is of the formula:

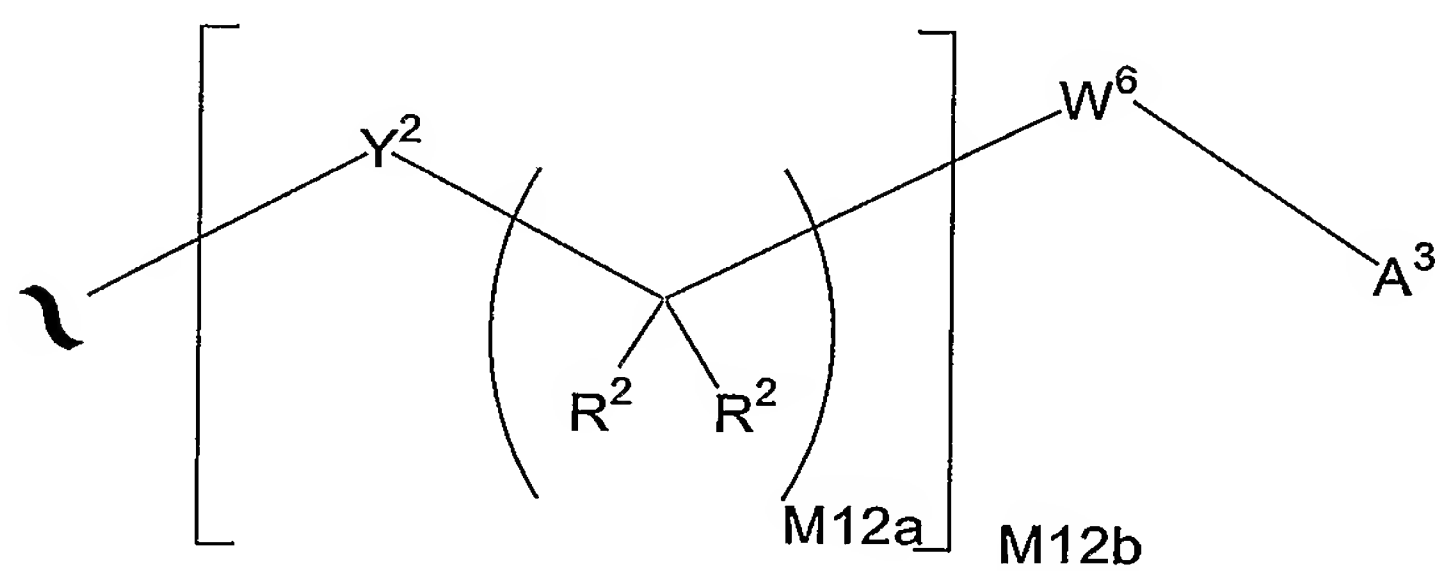


7. The compound of claim 5 wherein  $A^1$  is of the formula:

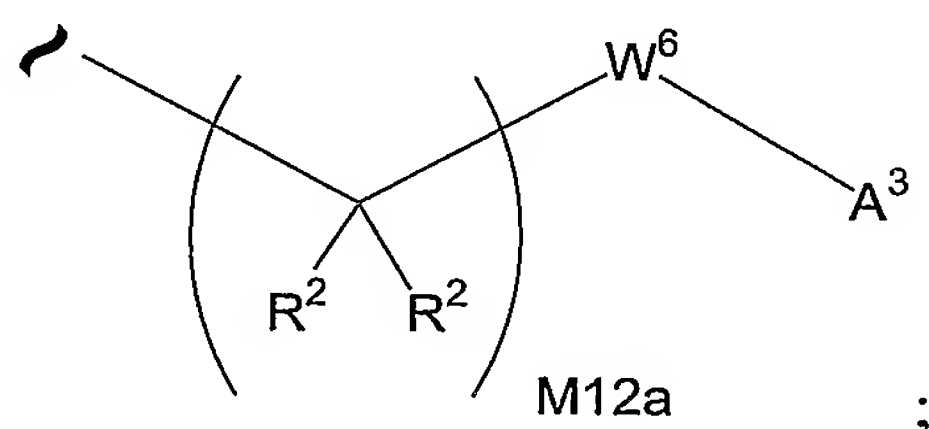


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8. The compound of claim 5 wherein  $A^1$  is of the formula:

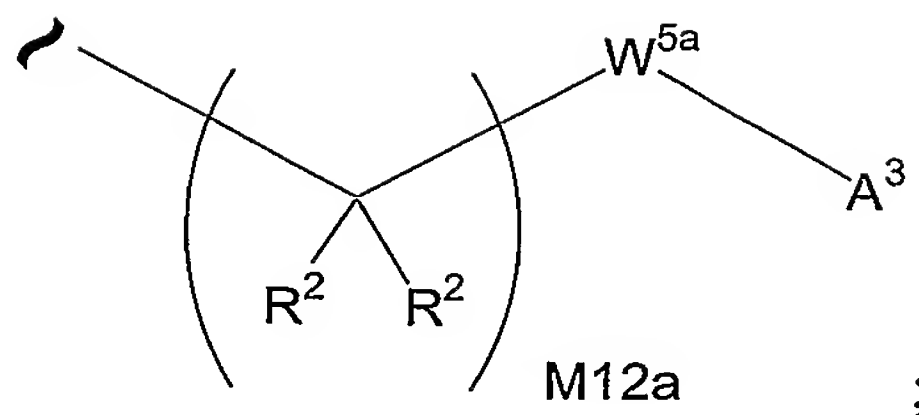


9. The compound of claim 5 wherein  $A^1$  is of the formula:



10

10. The compound of claim 5 wherein  $A^1$  is of the formula:

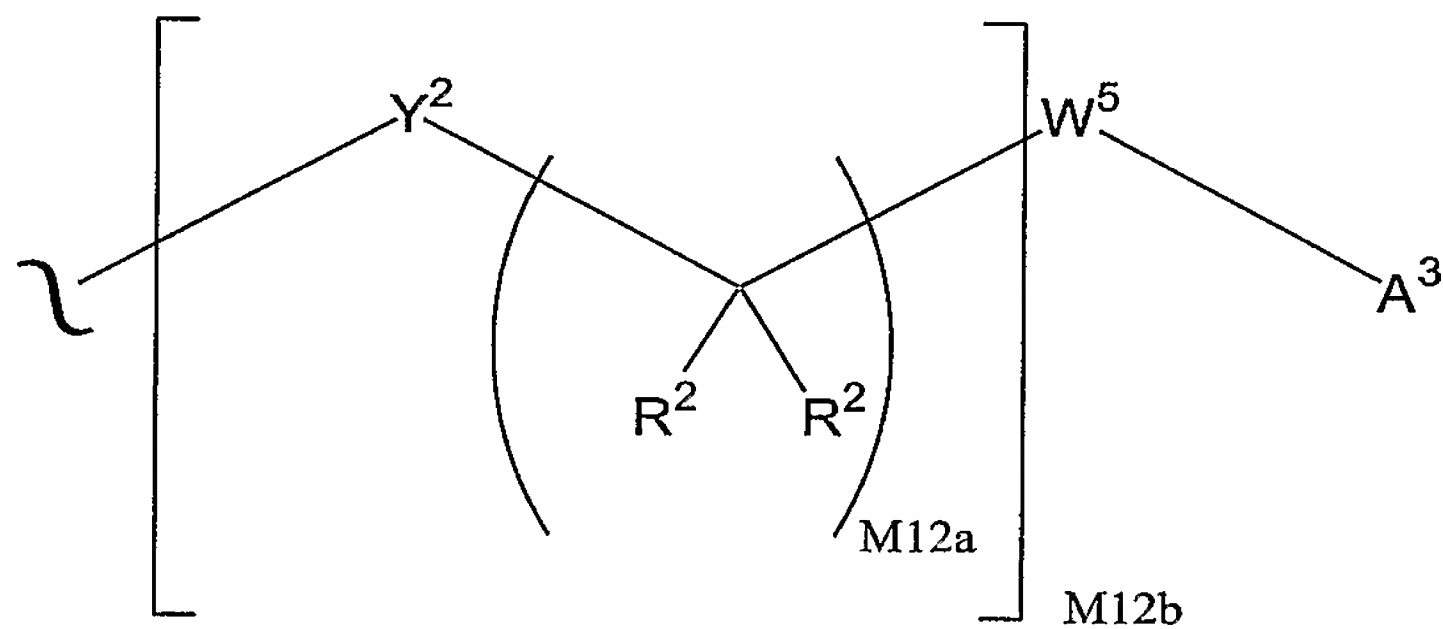


and  $W^{5a}$  is a carbocycle or a heterocycle where  $W^{5a}$  is independently substituted with 0 or 1  $R^2$  groups.

5

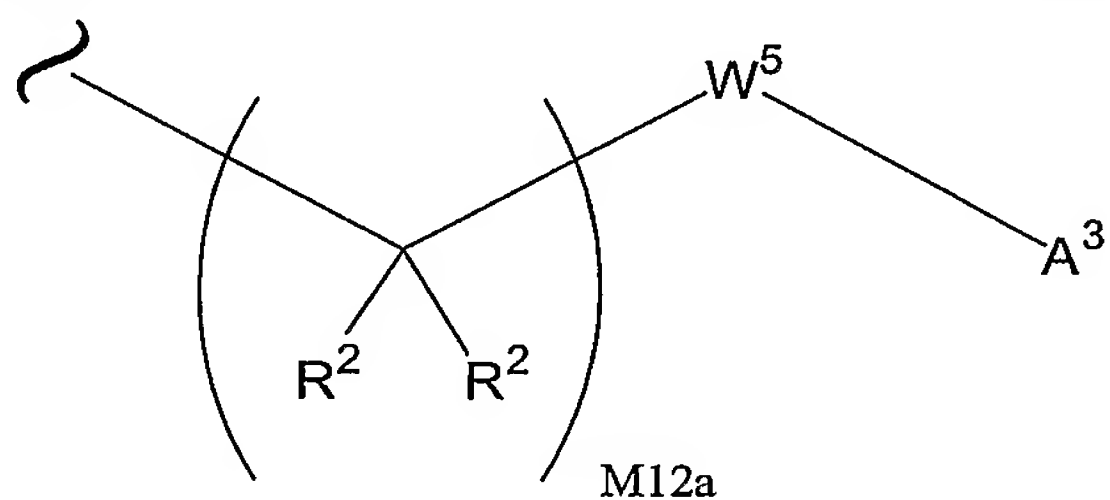
11. The compound of claim 5 wherein M12a is 1.

12. The compound of claim 5 wherein  $A^1$  is of the formula:

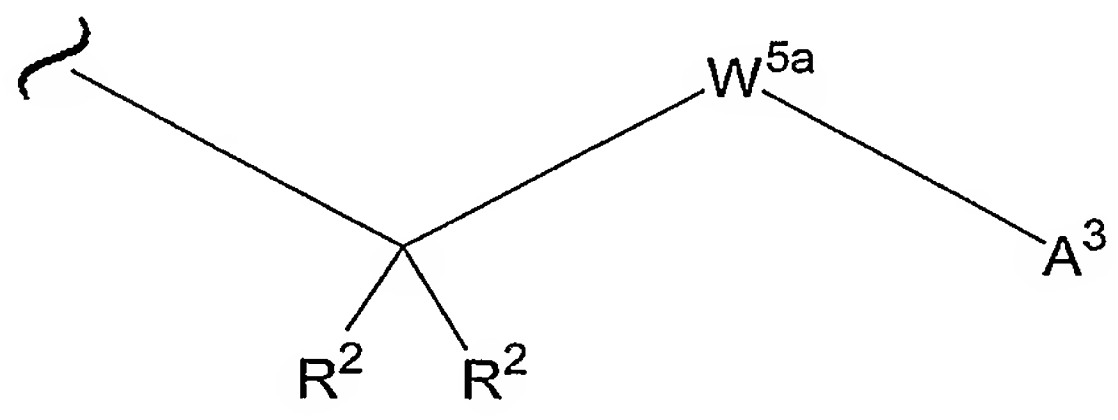


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13. The compound of claim 5 wherein  $A^1$  is of the formula:



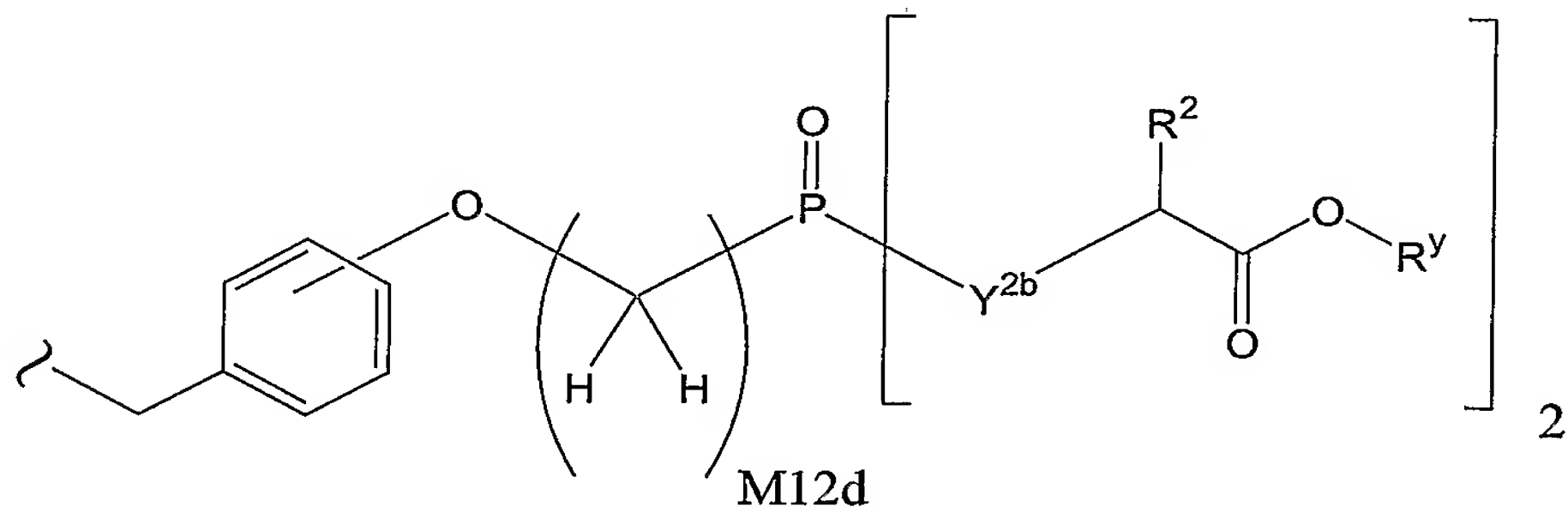
14. The compound of claim 5 wherein  $A^1$  is of the formula:



15

$W^{5a}$  is a carbocycle independently substituted with 0 or 1  $R^2$  groups;

15. The compound of claim 5 wherein  $A^1$  is of the formula:



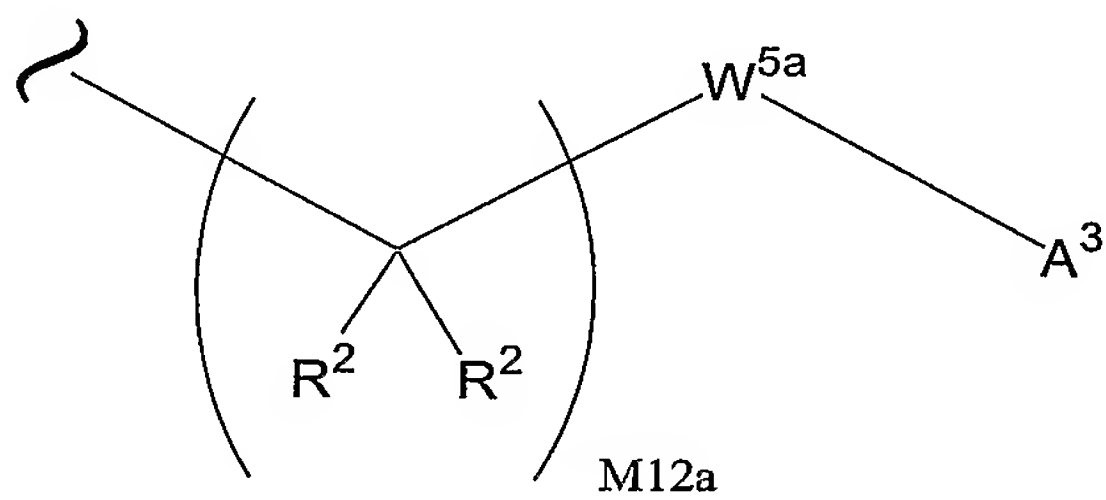
5

$Y^{2b}$  is O or  $N(R^2)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

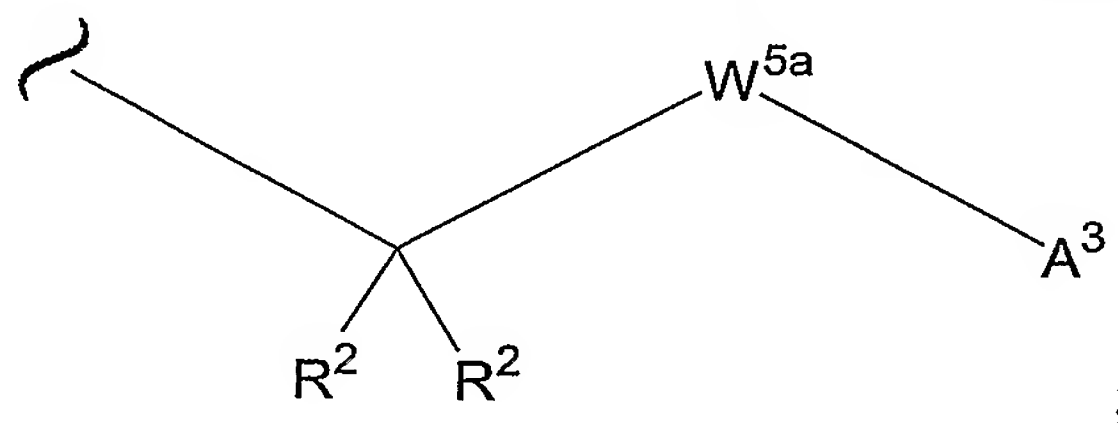
16. The compound of claim 5 wherein  $A^1$  is of the formula:

10



$W^{5a}$  is a carbocycle independently substituted with 0 or 1  $R^2$  groups;

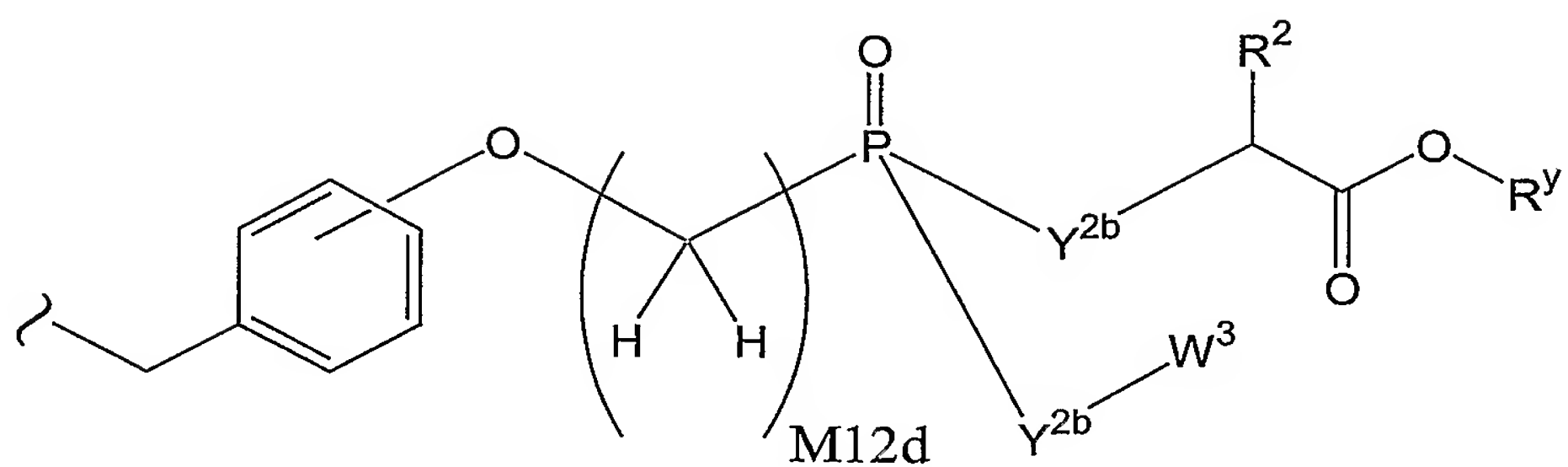
17. The compound of claim 5 wherein  $A^1$  is of the formula:



15

$W^{5a}$  is a carbocycle or heterocycle where  $W^{5a}$  is independently substituted with 0 or 1  $R^2$  groups.

- 20 18. The compound of claim 5 wherein  $A^1$  is of the formula:

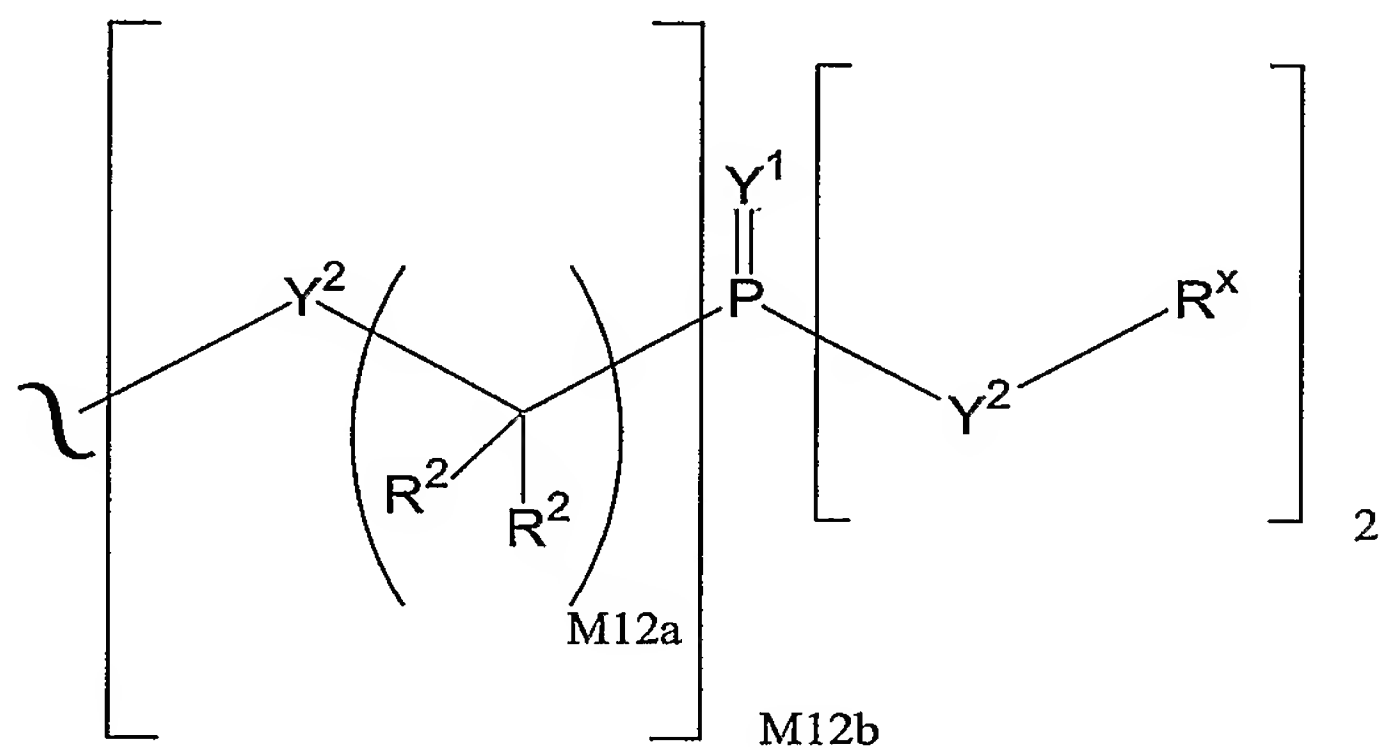


$Y^{2b}$  is O or  $N(R^2)$ ; and

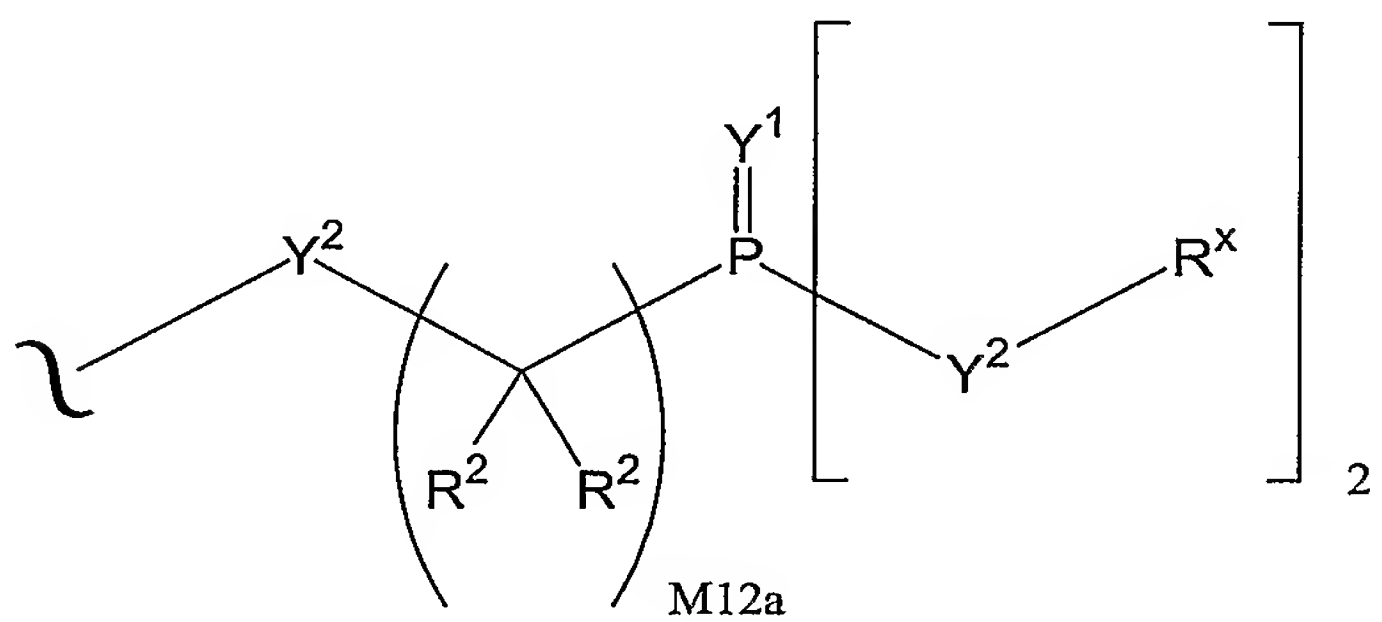
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

5

19. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



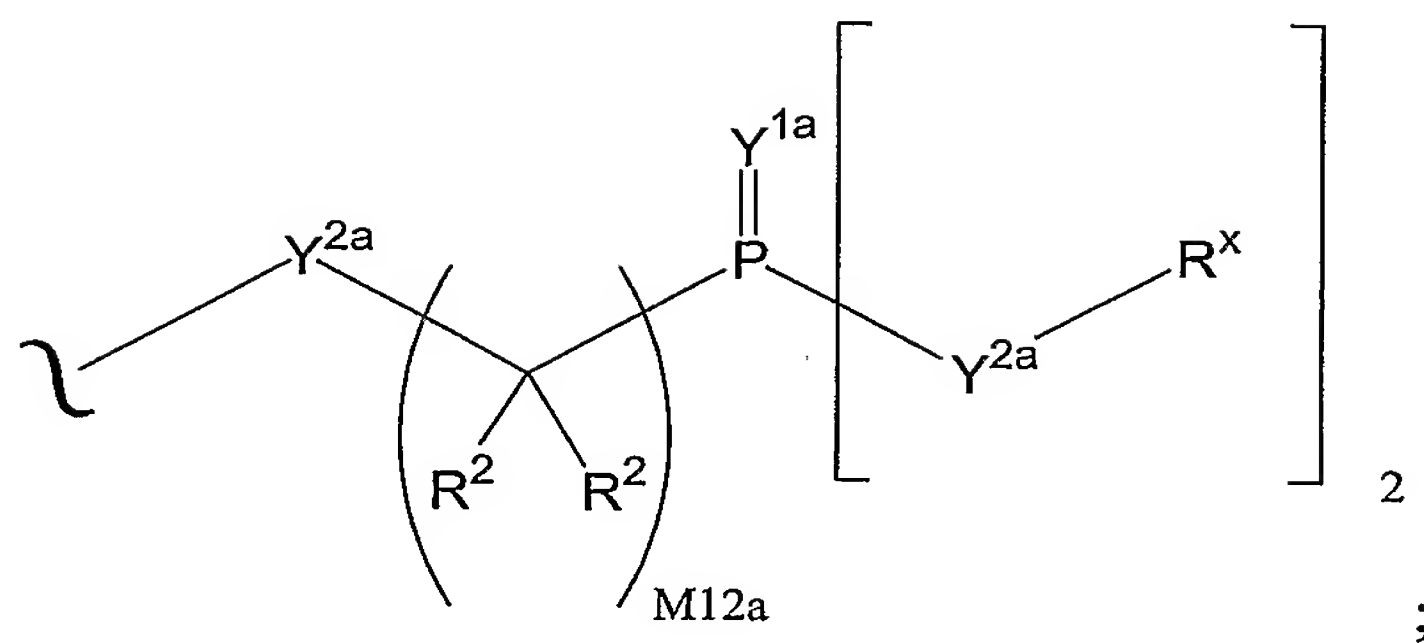
20. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



10

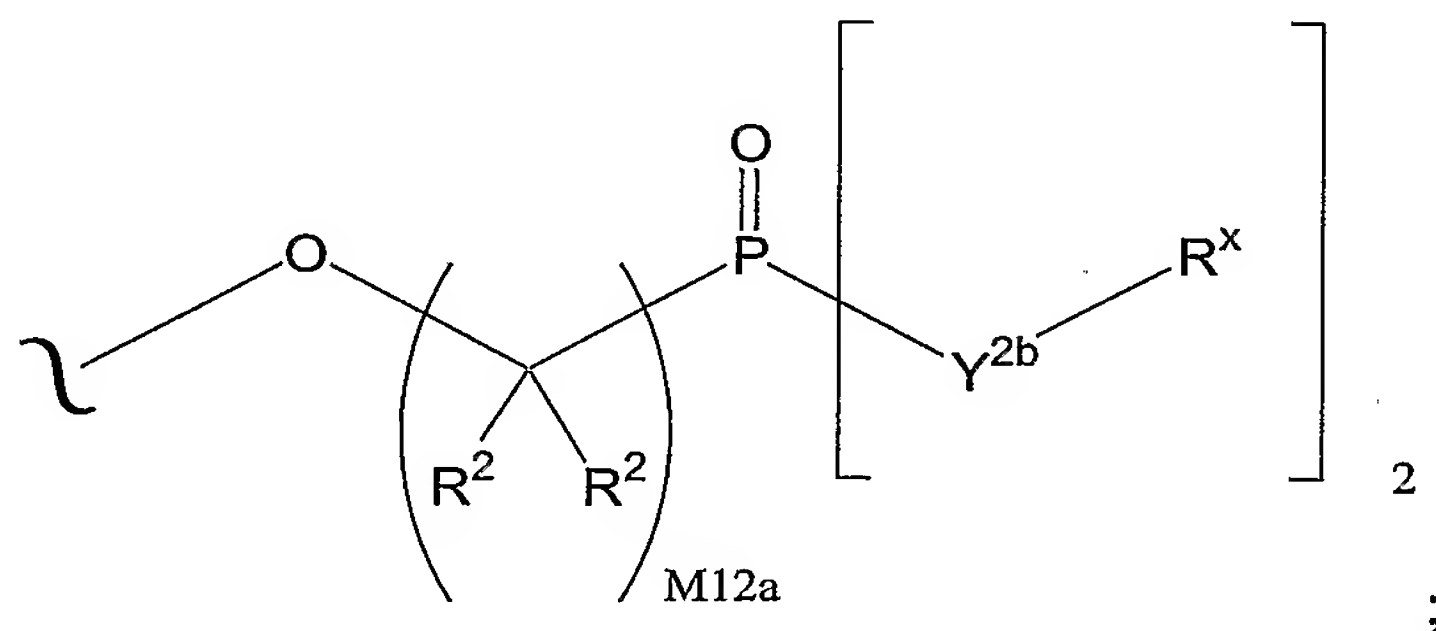
21. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:





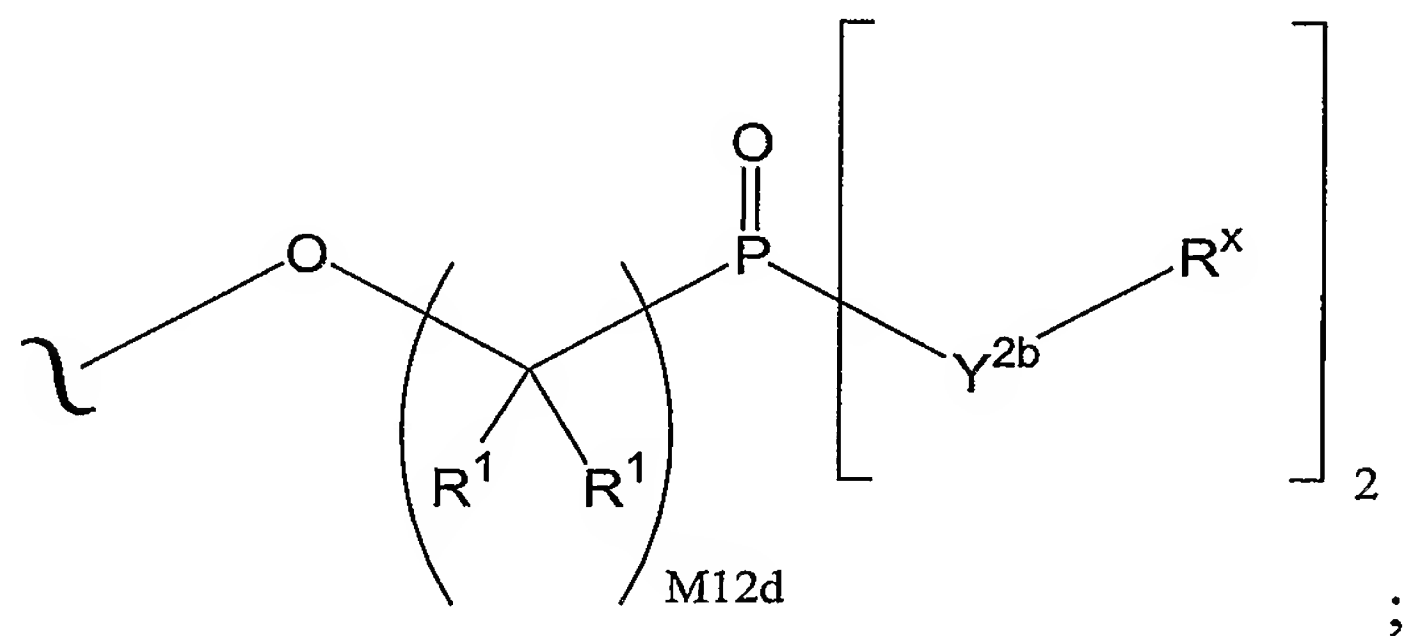
$Y^{1a}$  is O or S; and  
 $Y^{2a}$  is O, N(R<sup>x</sup>) or S.

- 5    22.    The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



and  $Y^{2b}$  is O or N(R<sup>x</sup>).

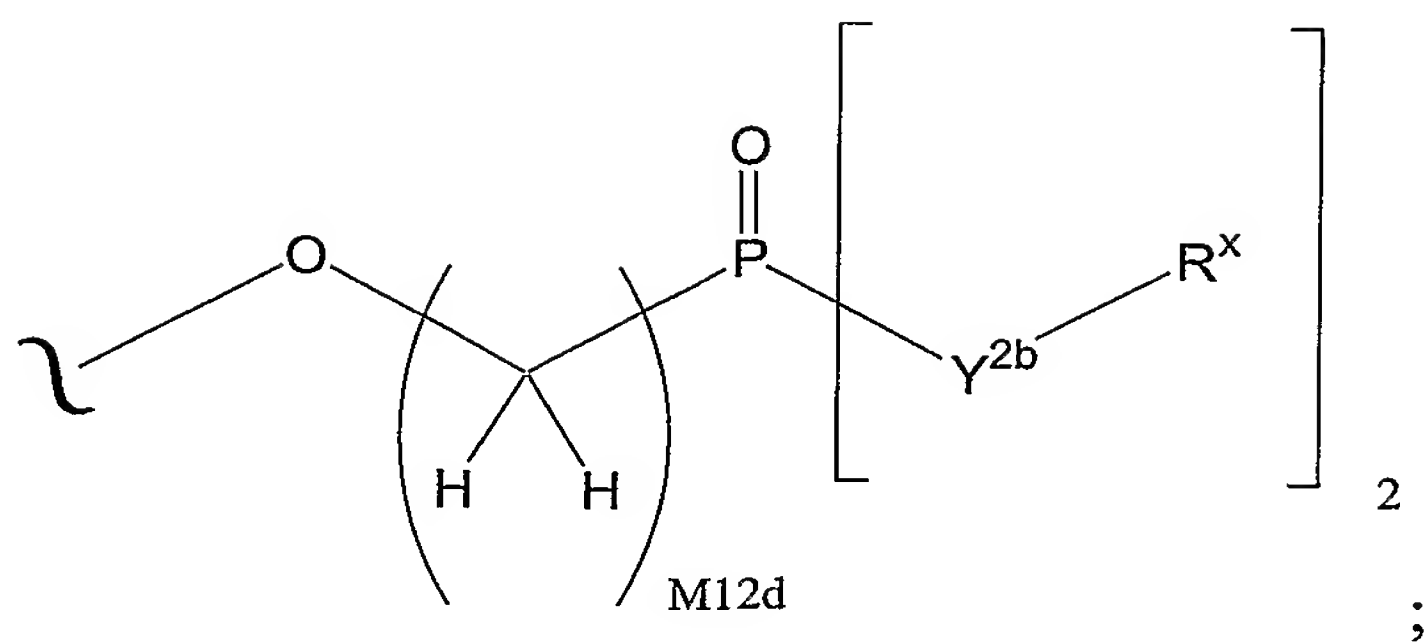
23.    The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



10

$R^1$  is independently H or alkyl of 1 to 18 carbon atoms;  
 $Y^{2b}$  is O or N(R<sup>x</sup>); and  
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

- 15    24.    The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:

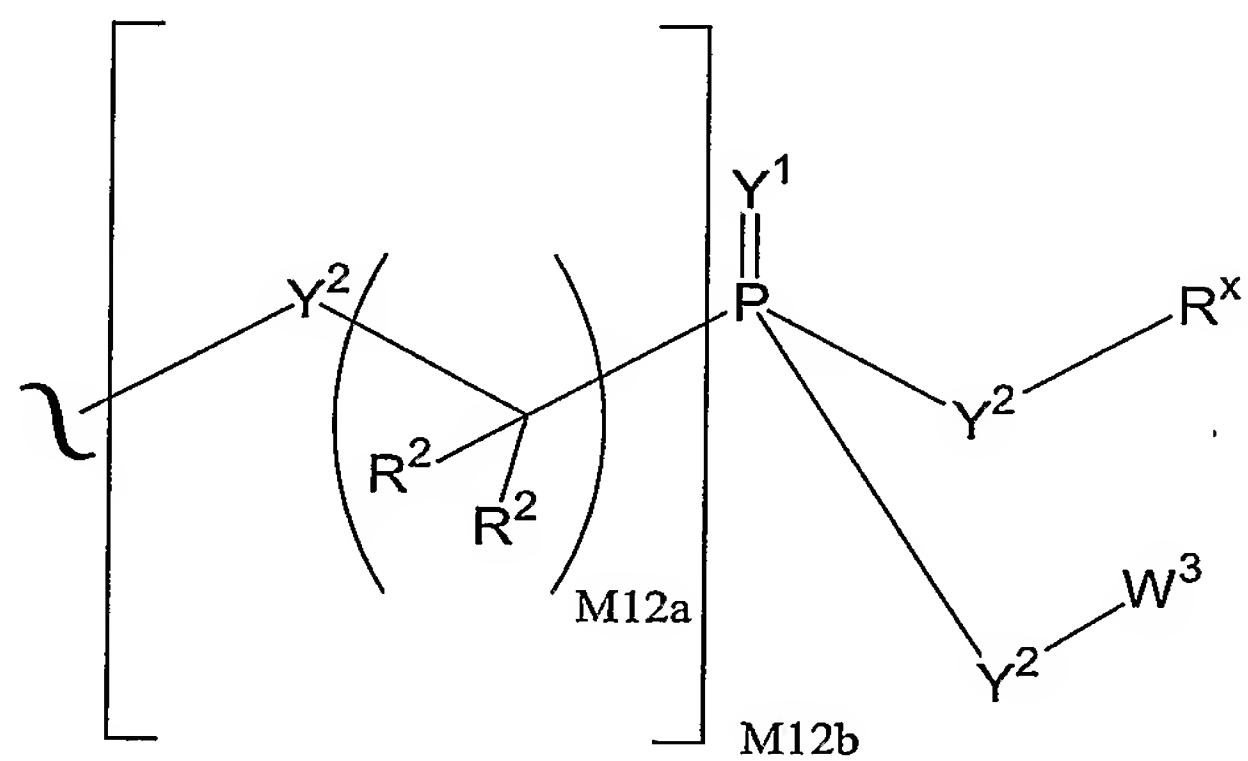


$Y^{2b}$  is O or  $N(R^x)$ ; and

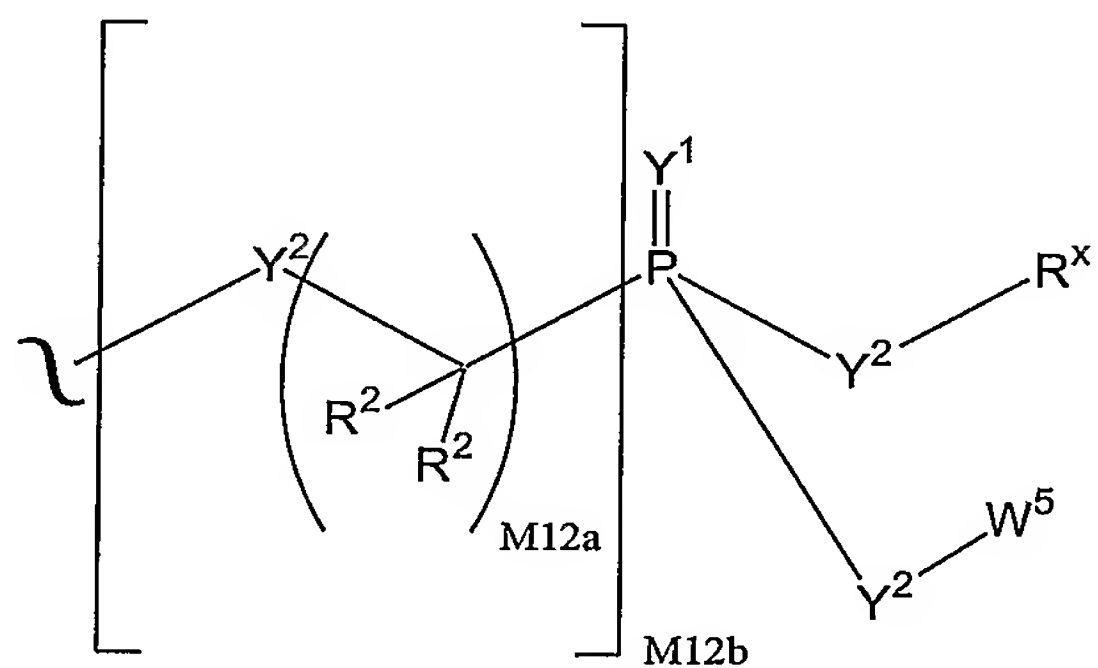
M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

5 25. The compound of claim 24 wherein M12d is 1.

26. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

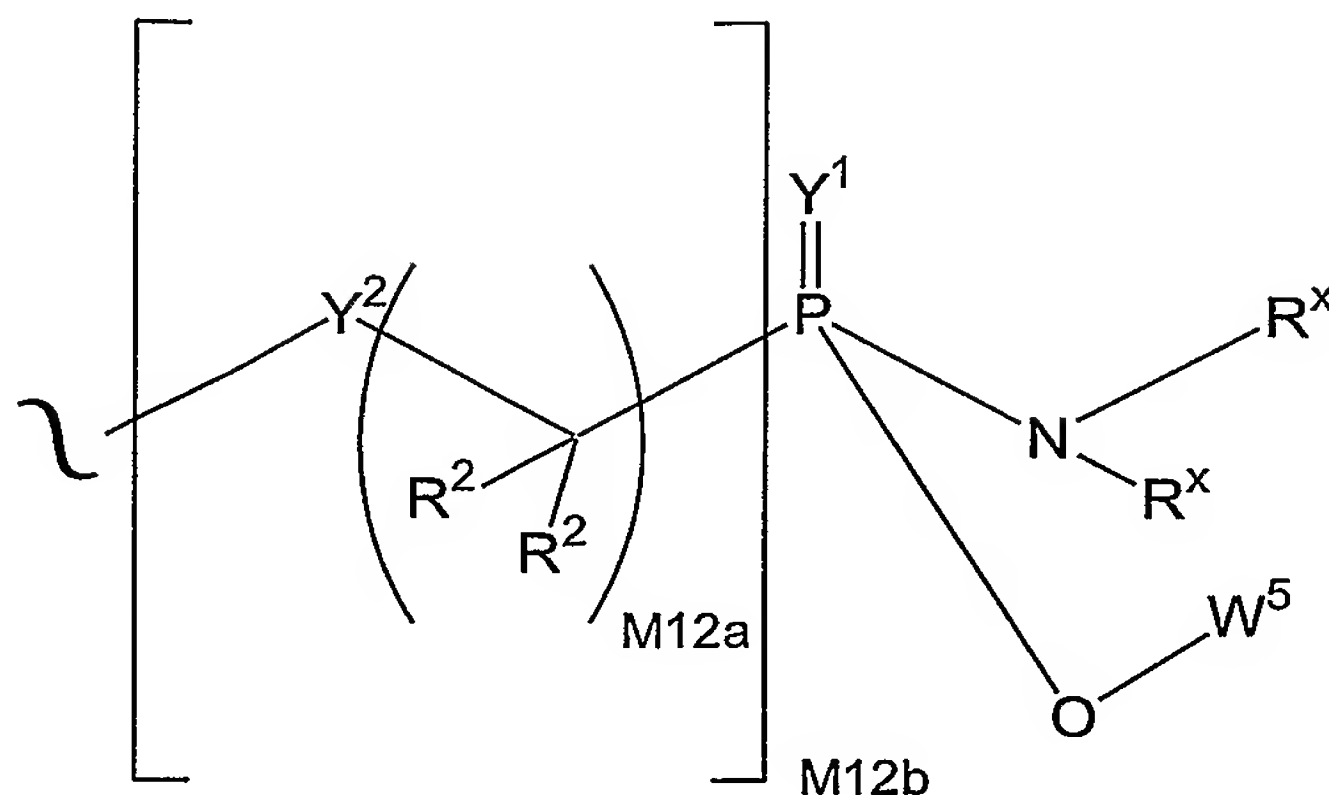


10 27. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



28. The compound of claim 27 wherein  $W^5$  is a carbocycle.

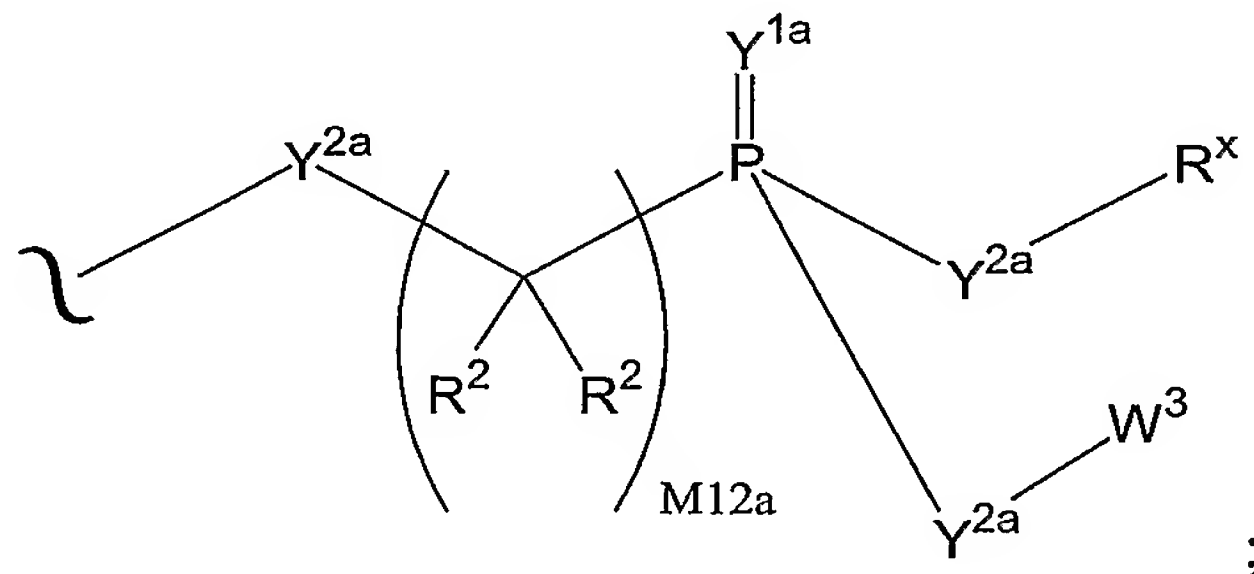
29. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



- 5 30. The compound of claim 29 wherein  $W^5$  is phenyl.

31. The compound of claim 30 wherein M12b is 1.

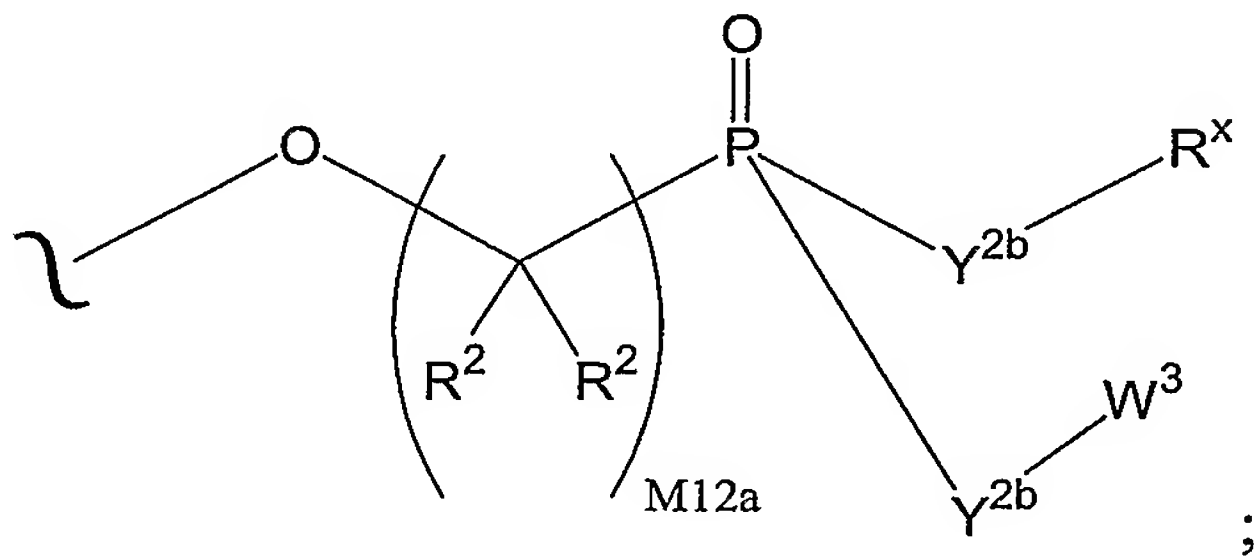
32. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



10

$Y^{1a}$  is O or S; and  
 $Y^{2a}$  is O,  $N(R^x)$  or S.

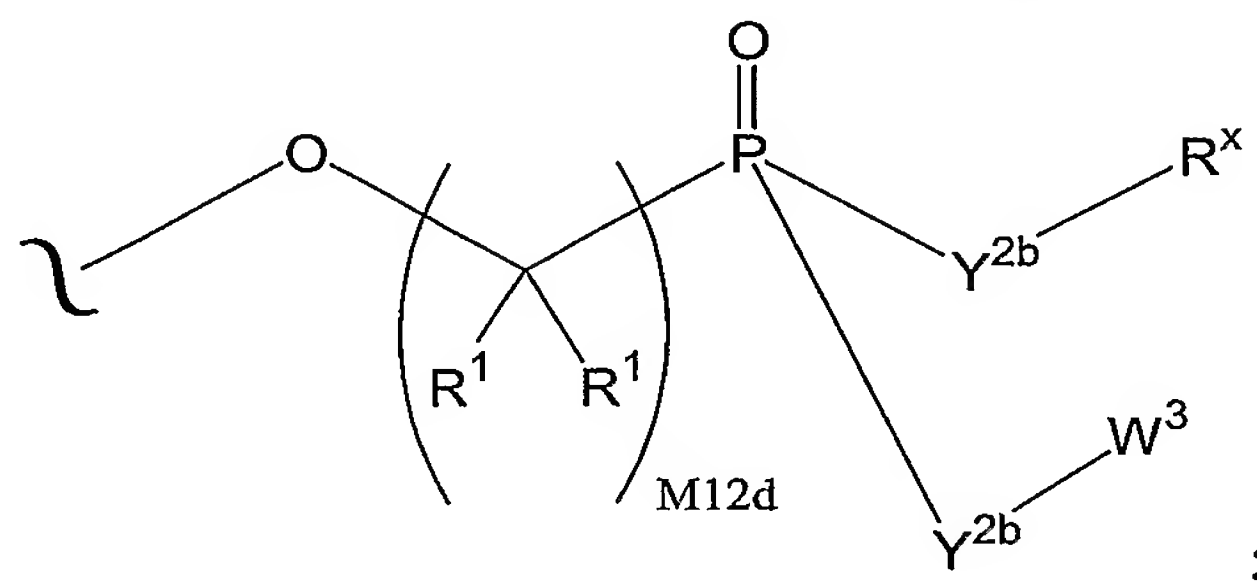
33. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



15

and  $Y^{2b}$  is O or  $N(R^x)$ .

34. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



$R^1$  is independently H or alkyl of 1 to 18 carbon atoms;

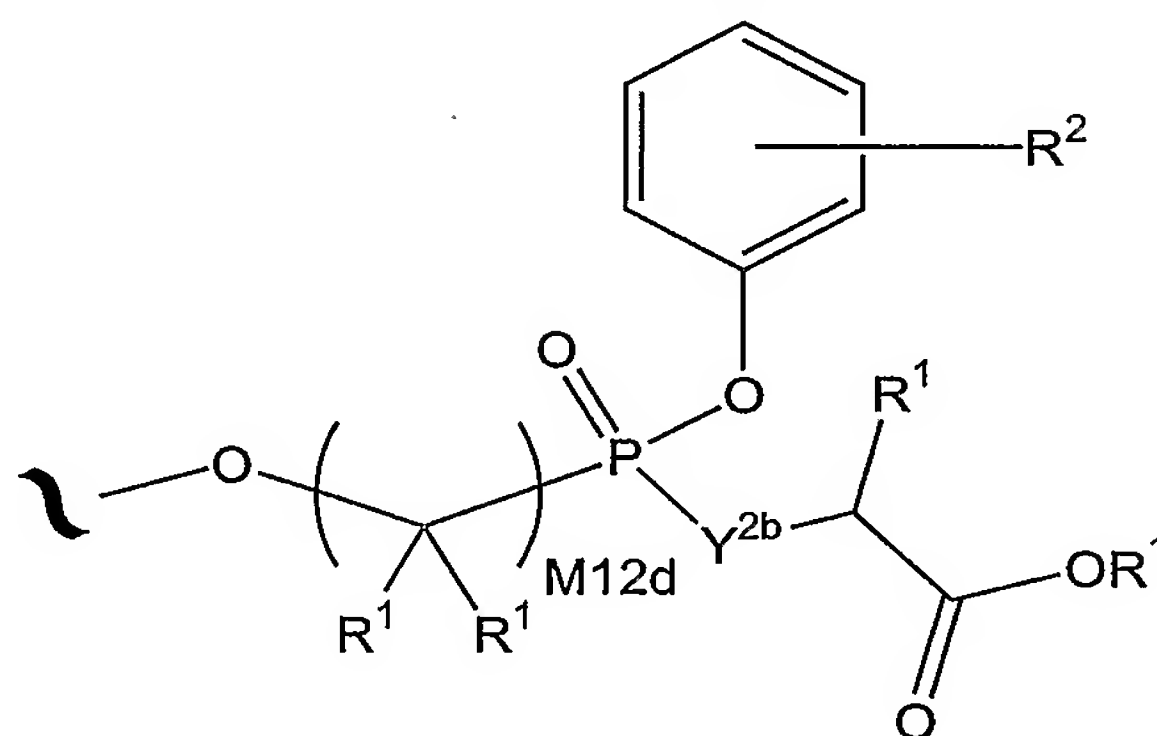
5  $Y^{2b}$  is O or  $N(R^x)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

35. The compound of claim 34 wherein  $R^1$  is H.

- 10 36. The compound of claim 34 wherein M12d is 1.

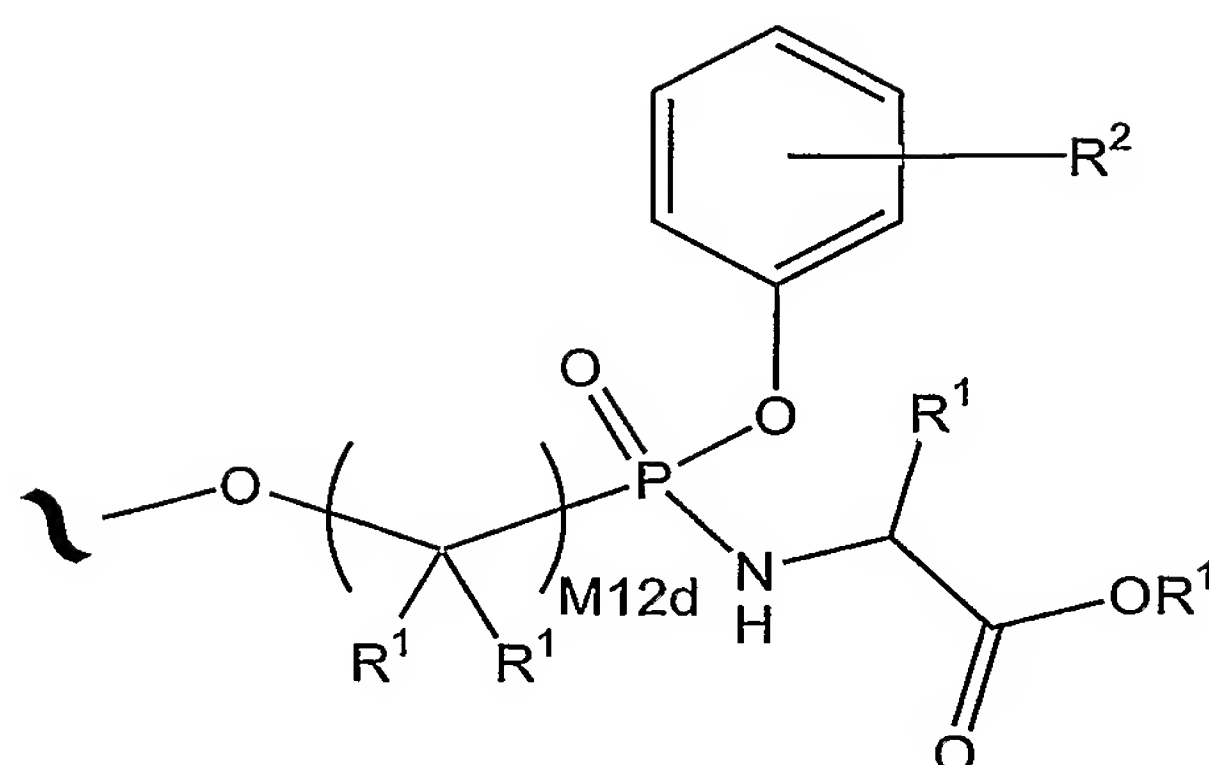
37. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



wherein the phenyl carbocycle is substituted with 0, 1, 2, or 3  $R^2$  groups.

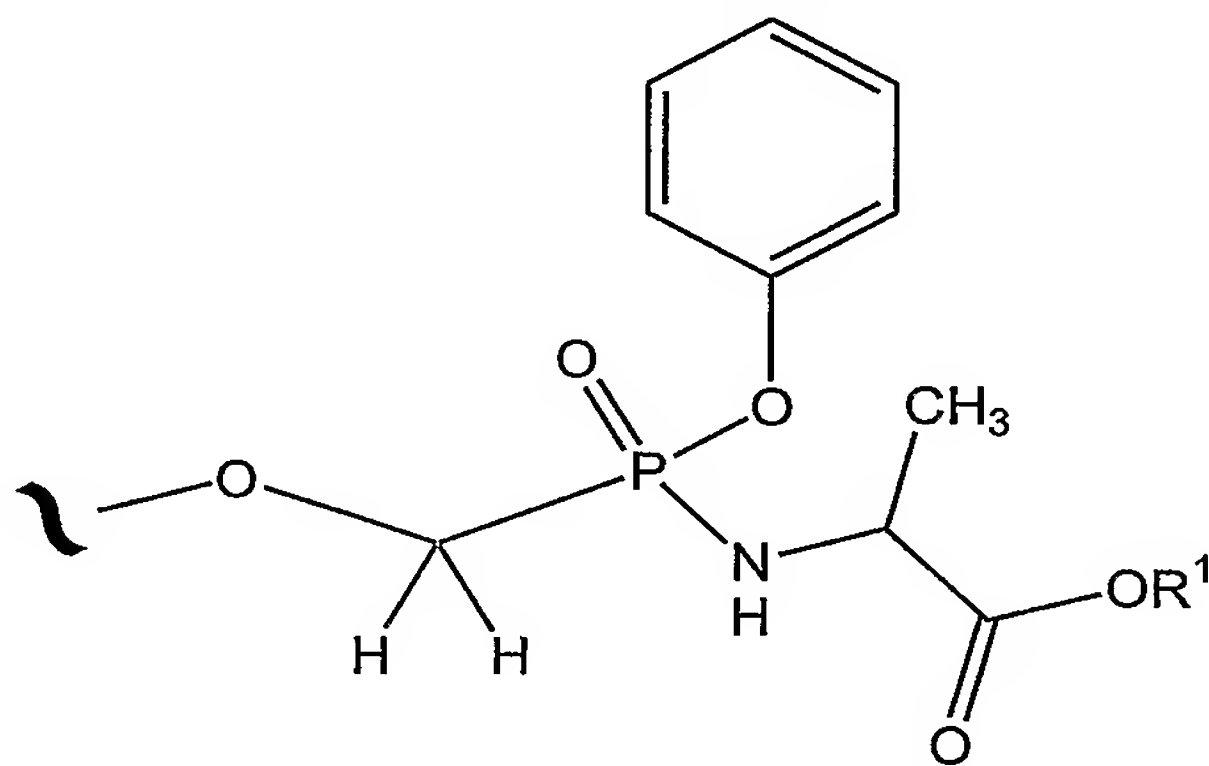
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38. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



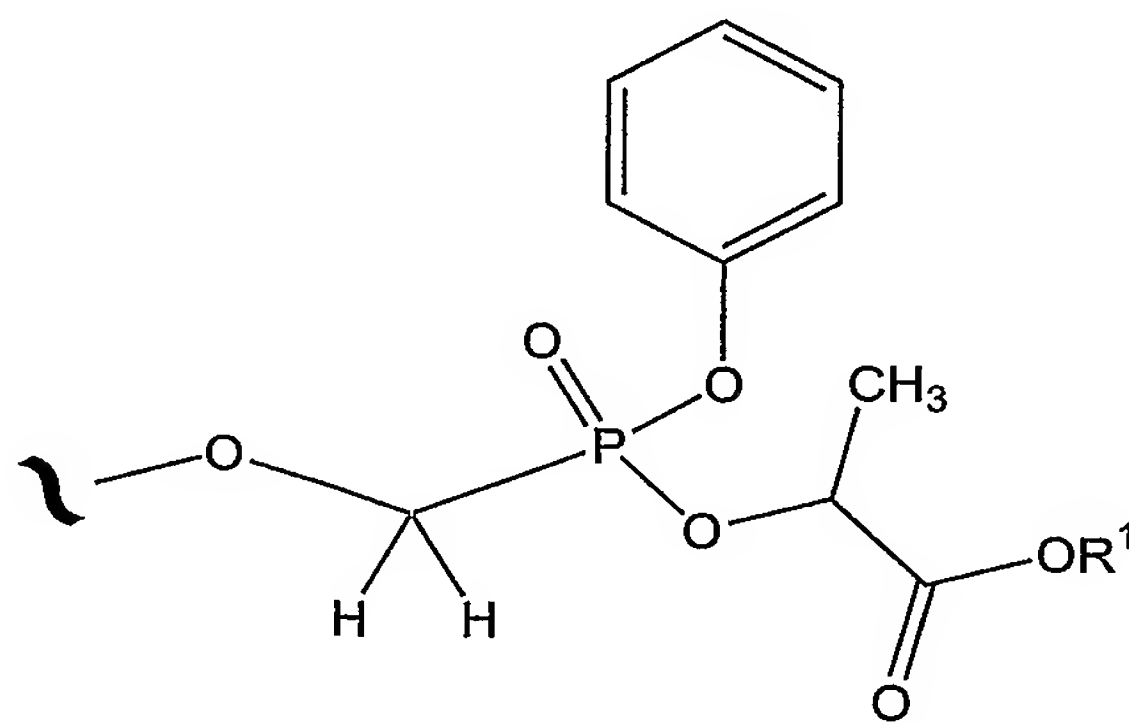
wherein  $R^1$  is independently H or alkyl of 1 to 18 carbon atoms.

39. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

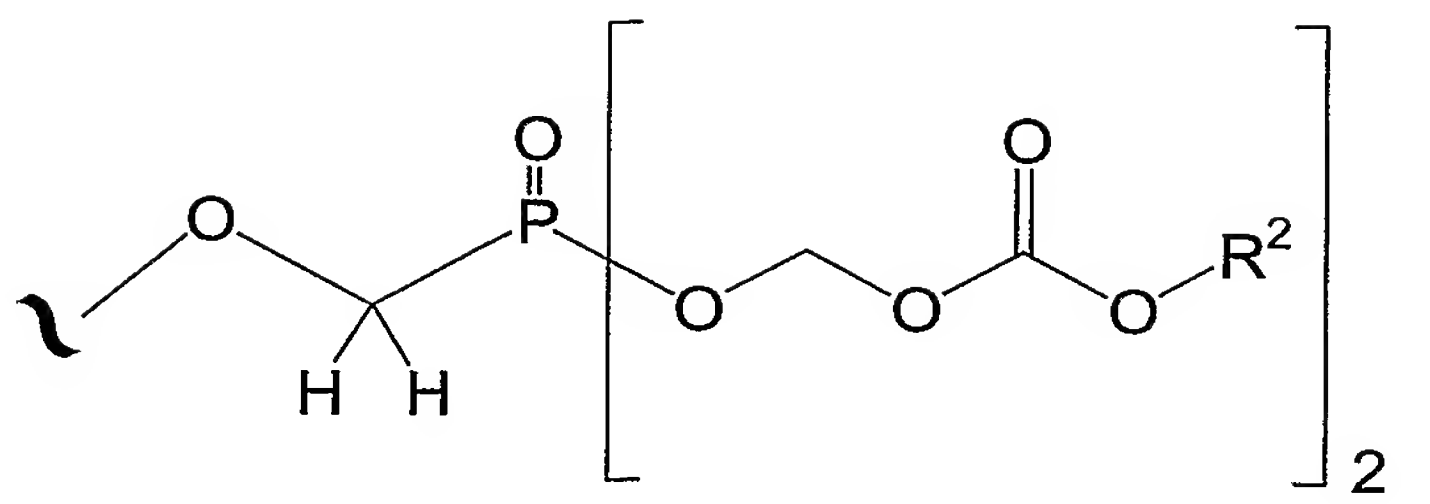


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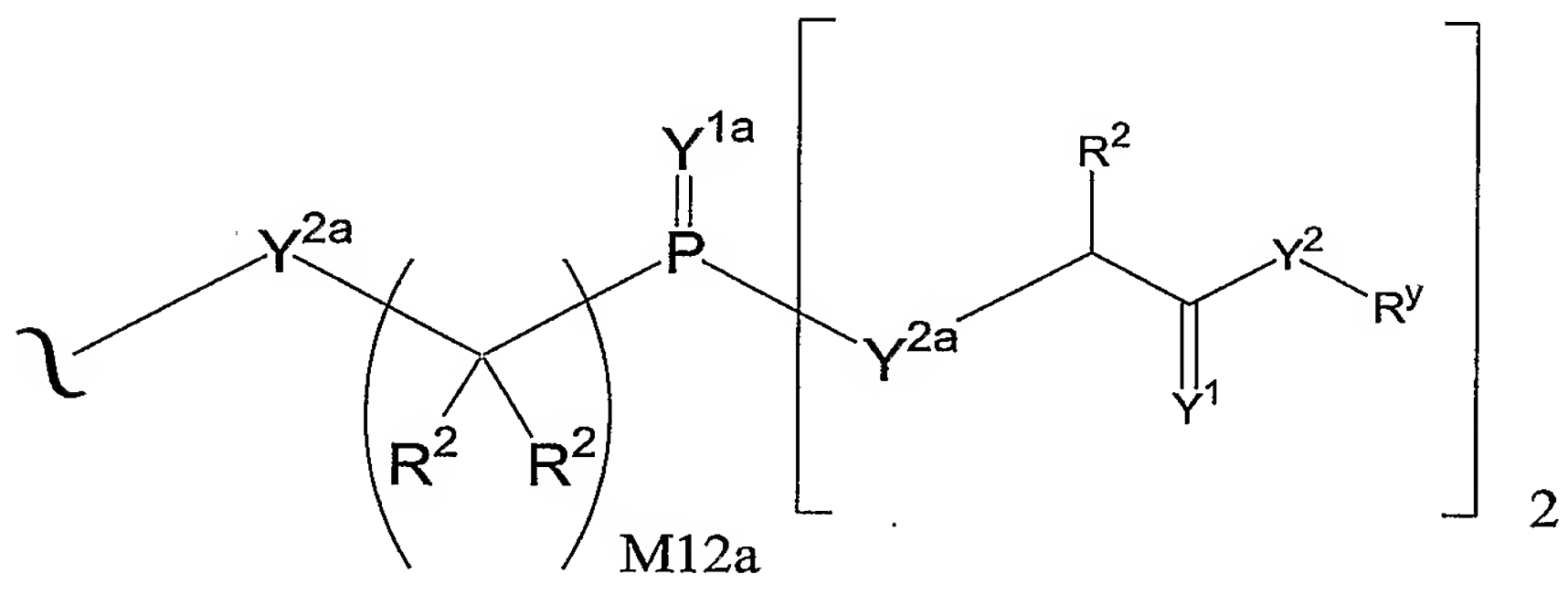
40. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



10 41. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



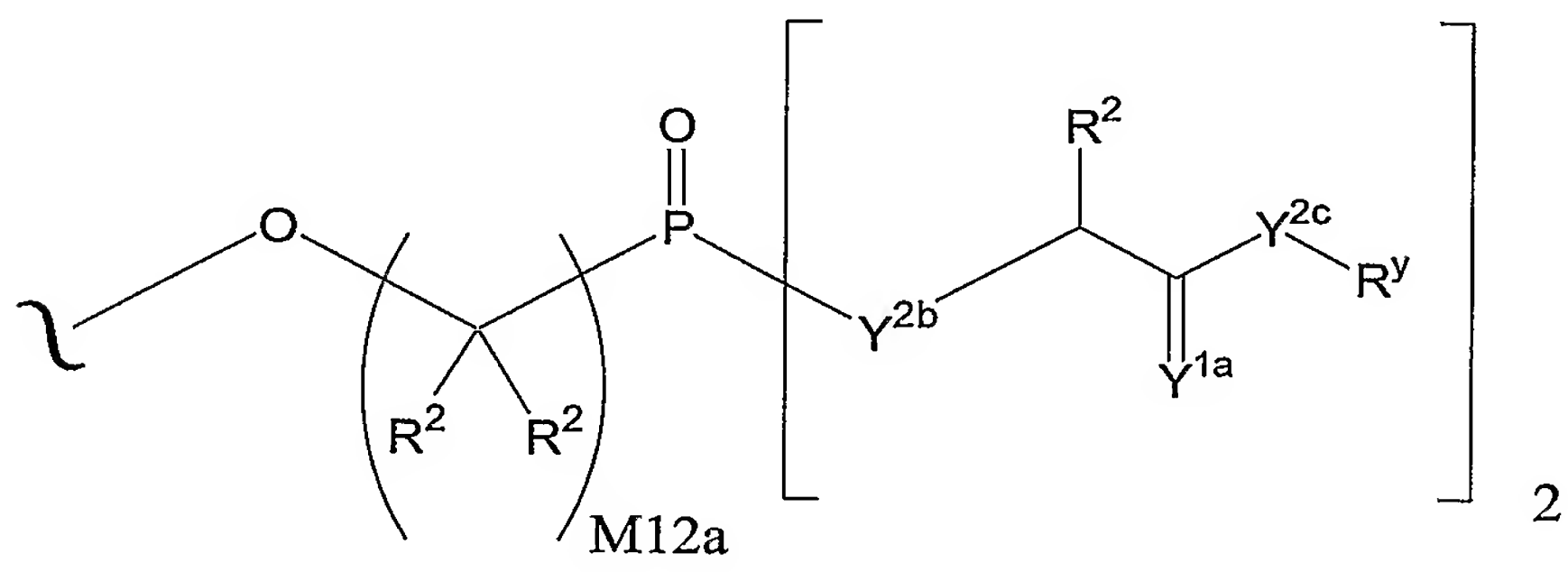
42. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



5

$Y^{1a}$  is O or S; and  
 $Y^{2a}$  is O,  $N(R^2)$  or S.

43. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

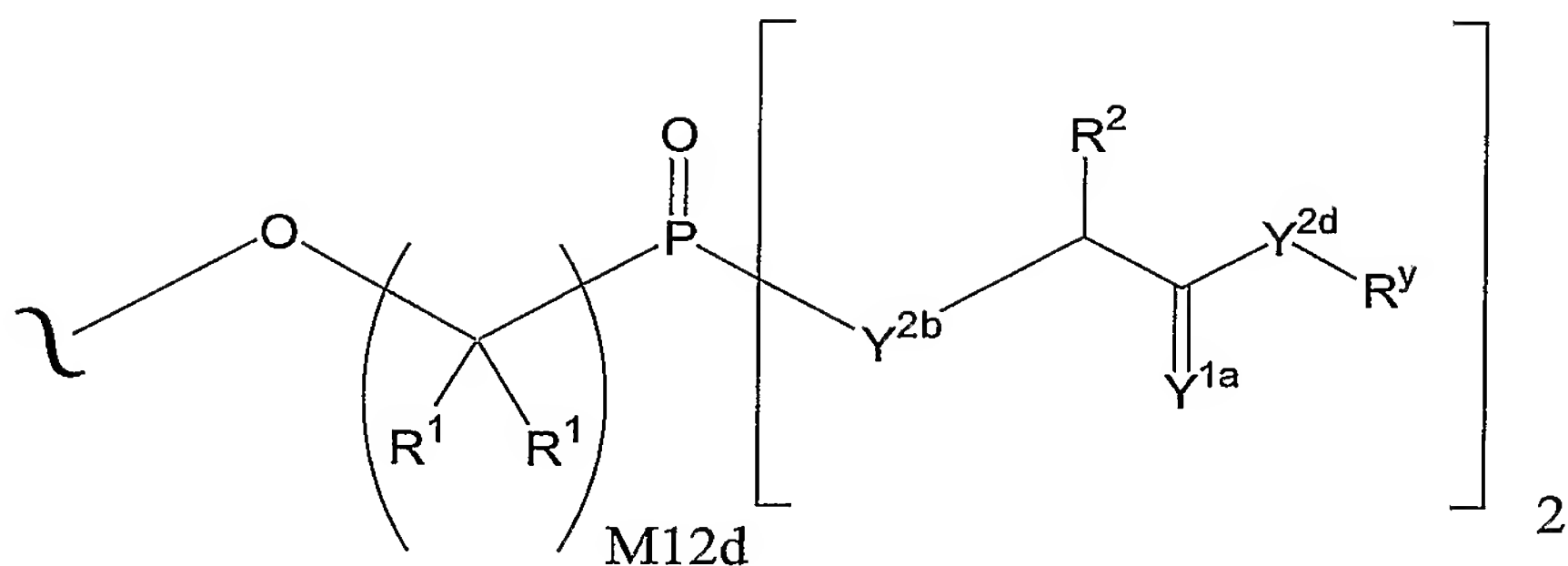


10

$Y^{1a}$  is O or S;  
 $Y^{2b}$  is O or  $N(R^2)$ ; and  
 $Y^{2c}$  is O,  $N(R^y)$  or S.

15

44. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



$R^1$  is independently H or alkyl of 1 to 18 carbon atoms;

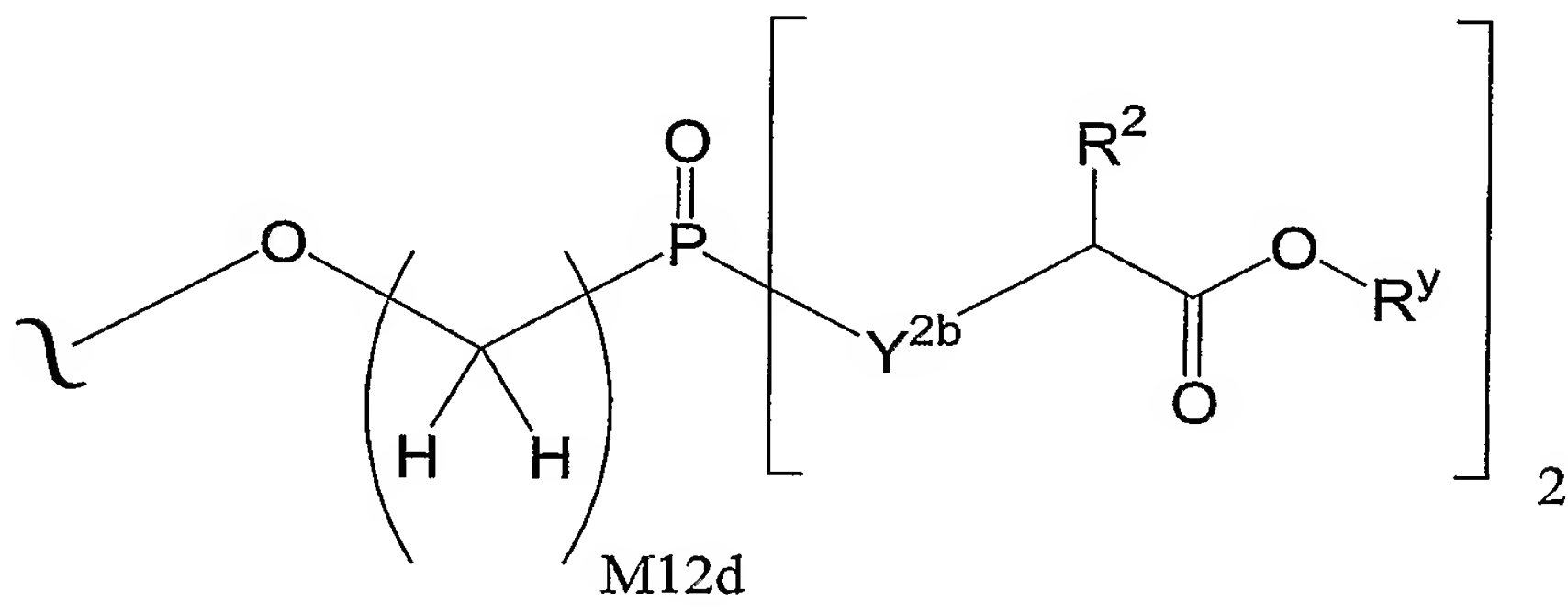
$Y^{1a}$  is O or S;

$Y^{2b}$  is O or  $N(R^2)$ ;

5  $Y^{2d}$  is O or  $N(R^y)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

45. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

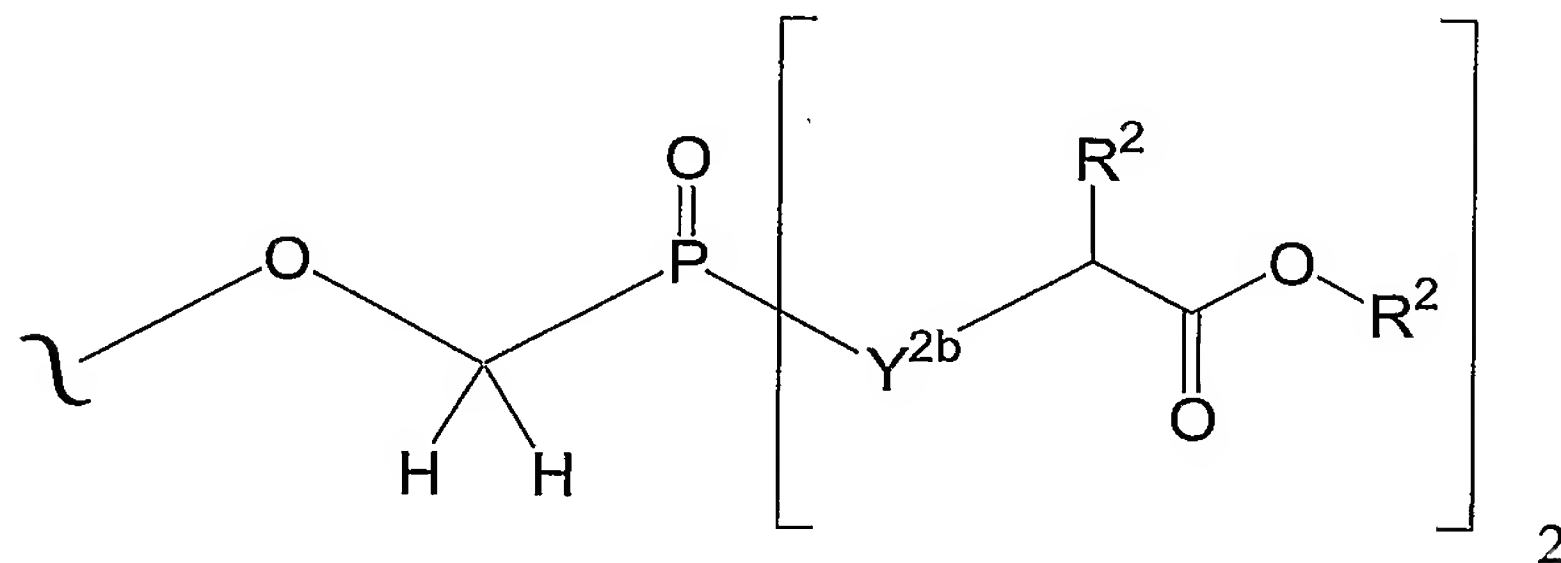


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$Y^{2b}$  is O or  $N(R^2)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

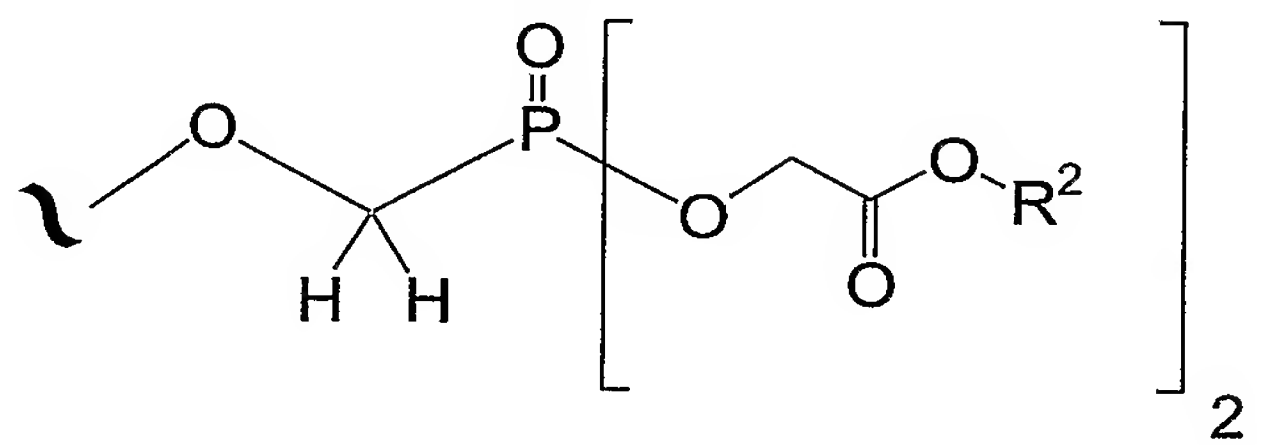
46. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



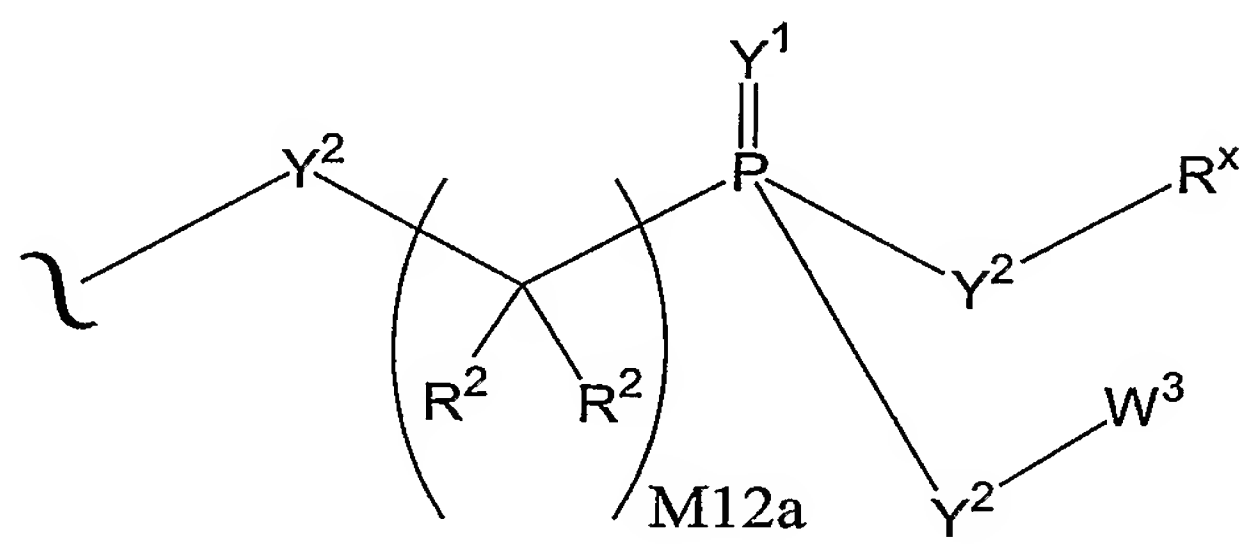
15

and  $Y^{2b}$  is O or  $N(R^2)$ .

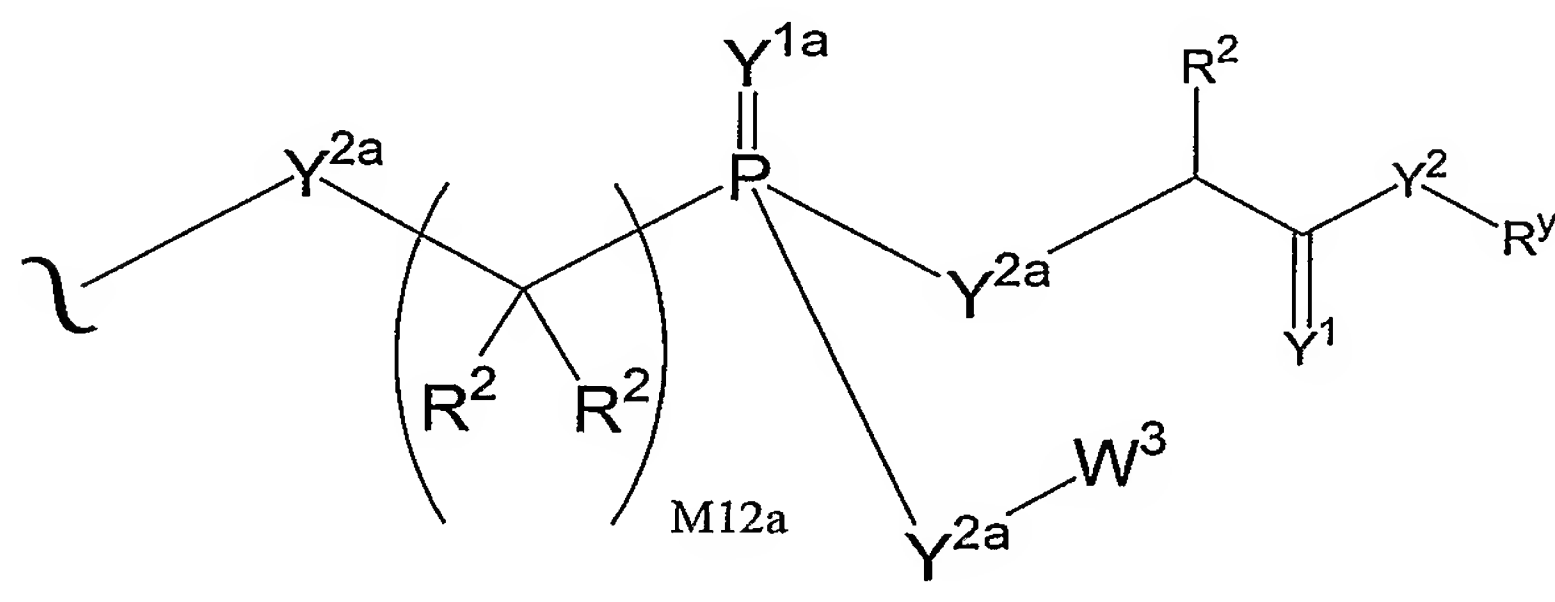
47. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



- 5 48. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



49. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:

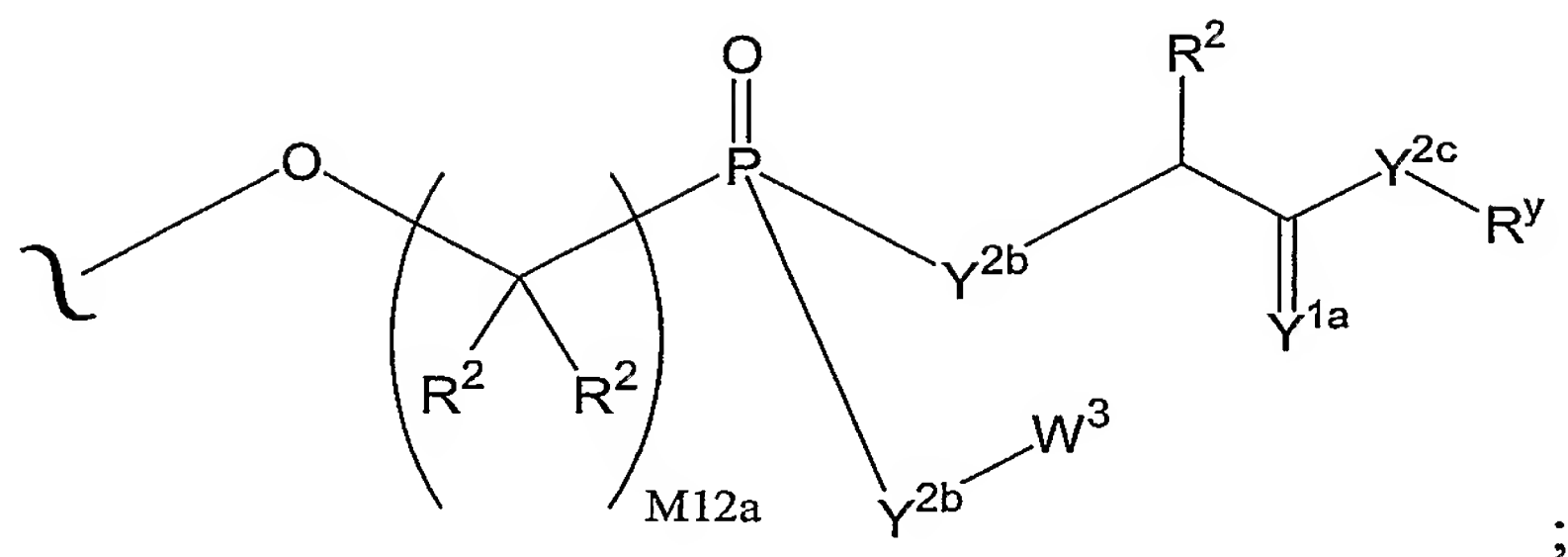


$Y^{1a}$  is O or S; and

$Y^{2a}$  is O,  $N(R^2)$  or S.

50. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:





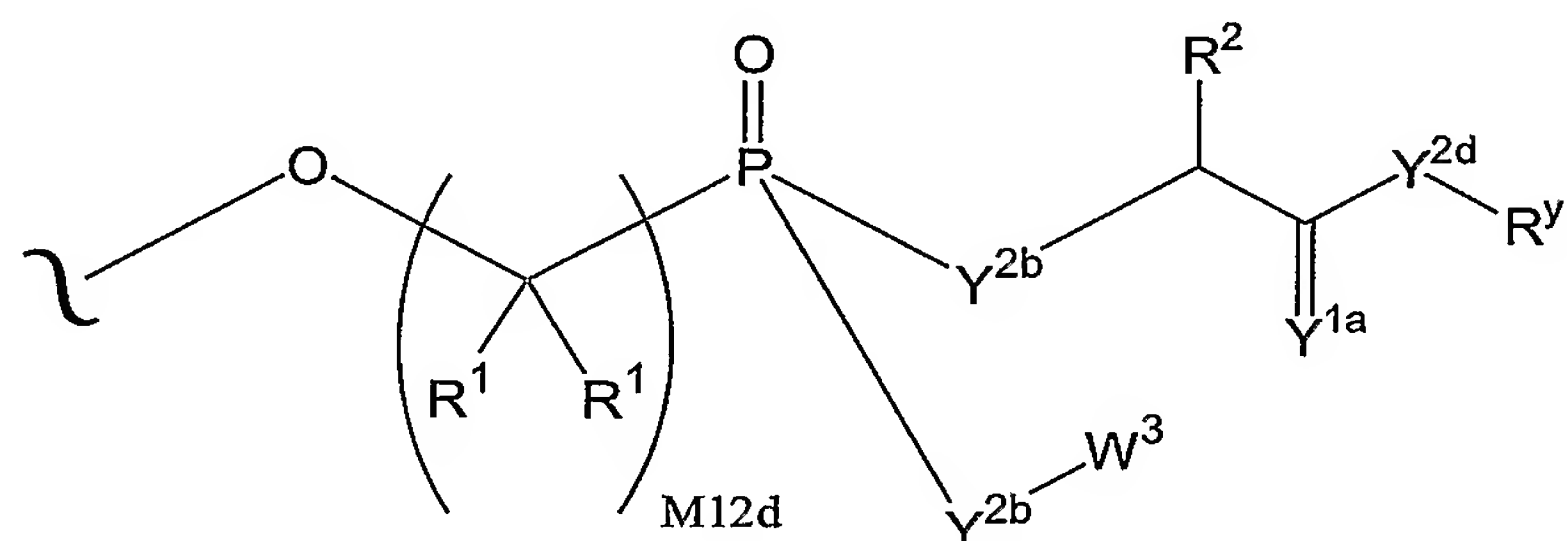
$Y^{1a}$  is O or S;

$Y^{2b}$  is O or  $N(R^2)$ ; and

$Y^{2c}$  is O,  $N(R^y)$  or S.

5

51. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



$R^1$  is independently H or alkyl of 1 to 18 carbon atoms;

$Y^{1a}$  is O or S;

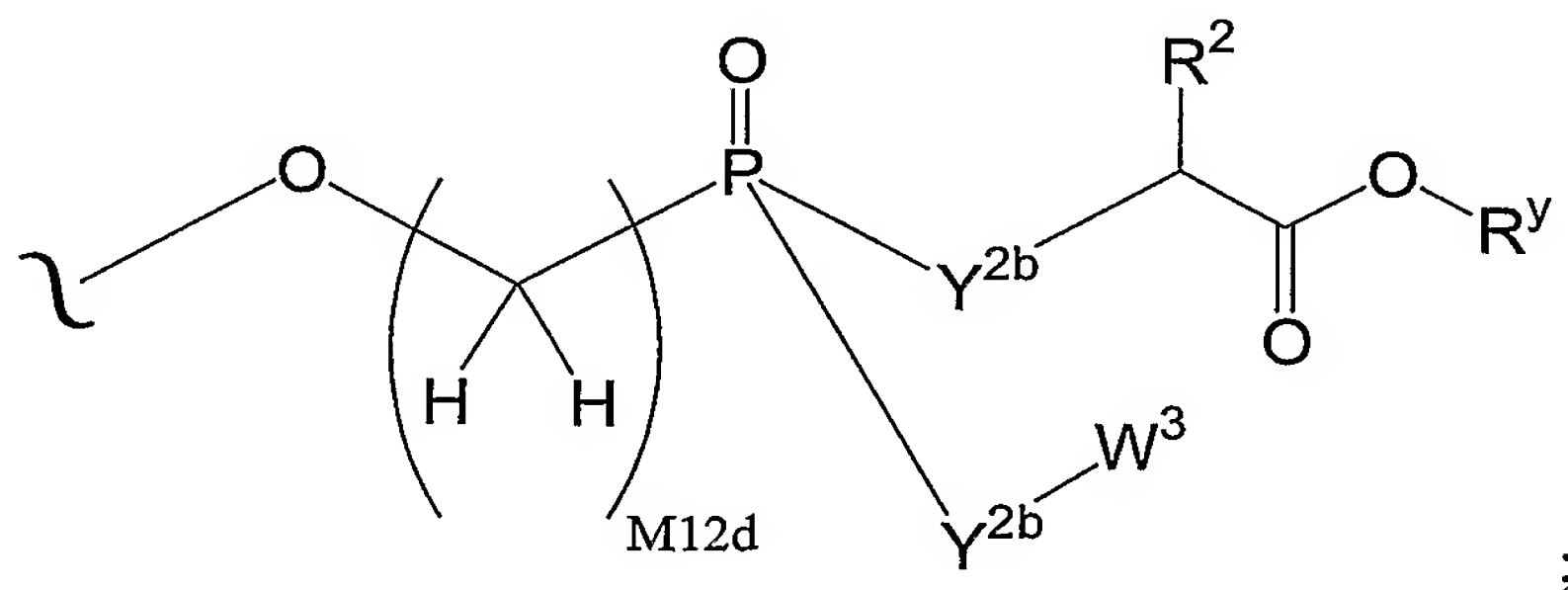
$Y^{2b}$  is O or  $N(R^2)$ ;

$Y^{2d}$  is O or  $N(R^y)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

10

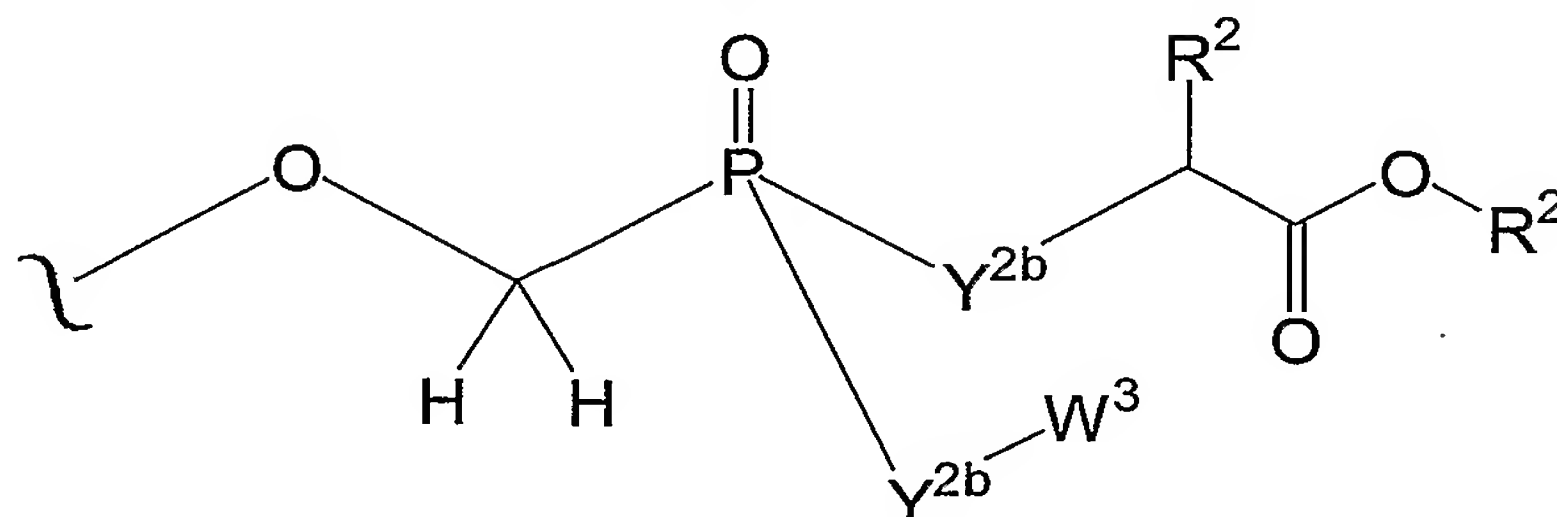
15 52. The compound of any one of claims 5-18 wherein  $A^3$  is of the formula:



$Y^{2b}$  is O or  $N(R^2)$ ; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

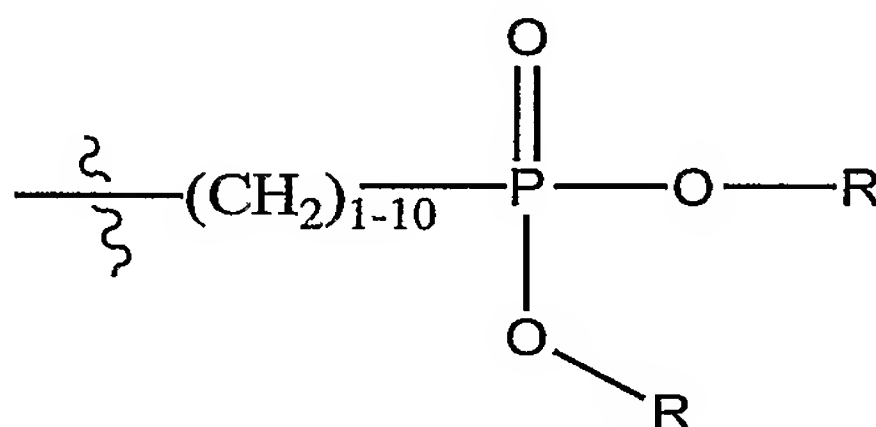
53. The compound of any one of claims 5-18 wherein A<sup>3</sup> is of the formula:



and Y<sup>2b</sup> is O or N(R<sup>2</sup>).

5

54. The compound of claim 5 wherein A<sup>0</sup> is of the formula:



wherein each R is independently (C<sub>1</sub>-C<sub>6</sub>)alkyl.

10

55. The compound of claim 2 wherein:

R<sup>a</sup> is hydrogen, or substituted aryl;

R<sup>20</sup> is hydrogen, cycloalkyl, or -NR<sup>b</sup>R<sup>c</sup>;

R<sup>b</sup> is hydrogen, and R<sup>c</sup> is substituted alkyl, or substituted aryl;

15 R<sup>21</sup> is hydrogen, alkyl, substituted cycloalkyl, or substituted aralkyl;

R<sup>22</sup> is hydrogen, or alkyl; and

R<sup>23</sup> is hydrogen, substituted aryl, substituted cycloalkyl, or aralkyl.

20 56. The compound of any one of claims 1-55 which inhibits a serine/threonine kinase, tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase, MAP Erk kinase, JAK3 kinase, VEGF receptor kinase, PDGF receptor tyrosine kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF receptor tyrosine kinase.

57. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound as described in any one of claims 1-55.

58. A unit dosage form comprising a compound as described in any one of  
5 claims 1-55 and a pharmaceutically acceptable excipient.

59. A method for inhibiting a kinase *in vitro* or *in vivo* comprising contacting a sample in need of such treatment with a compound as described in any one of claims 1-55.

10

60. The method of claim 59 wherein the contacting is *in vivo*.

61. A method of inhibiting a kinase in an animal, comprising administering a compound as described in any one of claims 1-55 to the animal.

15

62. The method of claim 61 wherein the compound is formulated with a pharmaceutically acceptable carrier.

63. The method of claim 62 wherein the formulation further comprises a  
20 second active ingredient.

64. The method of any one of claims 59-63 wherein the kinase is a serine/threonine kinase, tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase, MAP Erk kinase, JAK3 kinase, VEGF receptor  
25 kinase, PDGF receptor tyrosine kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF receptor tyrosine kinase.

65. A method of treating cancer in an animal in need of such treatment comprising administering an effective amount of a compound as described in  
30 any one of claims 1-55 to the animal.

66. A compound as described in any one of claims 1-55 for use in medical therapy.

67. The use of a compound as described in any one of claims 1-55 to prepare  
5 a medicament for inhibiting a kinase in an animal.

68. The use of claim 67 wherein the kinase is a serine/threonine kinase,  
tyrosine kinase, Bcr-Abl kinase, cyclin-dependent kinase, Flt3 tyrosine kinase,  
MAP Erk kinase, JAK3 kinase, VEGF receptor kinase, PDGF receptor tyrosine  
10 kinase, protein kinase C, insulin receptor tyrosine kinase, and/or an EGF  
receptor tyrosine kinase.

69. The use of a compound as described in any one of claims 1-55 to prepare  
a medicament for treating cancer in an animal.  
15

70. A method for preparing a compound as described in the schemes and  
examples herein.

71. A method for preparing a pharmaceutical composition, comprising  
20 combining a pharmaceutically acceptable excipient and a compound as  
described in any one of claims 1-55.